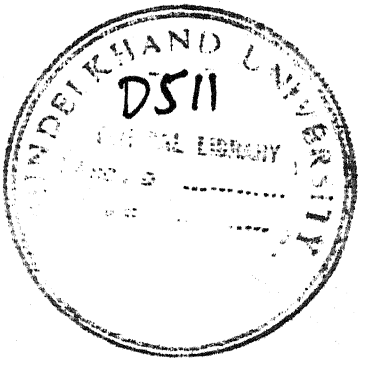
COMPARATIVE STUDY ON SERUM LIPID PROFILE IN FEMALES OF REPRODUCTIVE AGE GROUP USING DIFFERENT ORAL CONTRACEPTIVES- COMBINED PILLS, TRIPHASIC PILLS, CENTCHROMAN

THESIS

For

MASTER OF SURGERY

(OBSTETRICS & GYNAECOLOGY)



BUNDELKHAND UNIVERSITY
JHANSI (U. P.)

1995 **LOVELESH KUMARI BERIYA**

C O N T E N T S

C E R T I F I C A T E

This is to certify that the work entitled "COMPARATIVE STUDY ON SERUM LIPID LIPOPROTEIN PROFILE IN FEMALES OF REPRODUCTIVE AGE GROUP USING DIFFERENT ORAL CONTRACEPTIVES - COMBINED PILLS, TRIPHASIC PILLS AND CENTCHROMAN", which is being submitted as a thesis for M.S.(Obstetrics & Gynaecology), has been carried out by DR. LOVELESH KUMARI BERIA in the Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi.

She has put in the necessary stay in the department as per university regulations.

Dated :

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M.S.,
Associate Professor & Head,
Department of Obstetrics &
Gynaecology,
M.L.B. Medical College,
Jhansi.

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A C K N O W L E D G E M E N T

It is with an overwhelming sense of gratitude that I wish to acknowledge all those who made the completion of this thesis possible.

First and foremost is respected Dr.(Mrs.) Mridula Kapoor, M.S., Head, Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi who with her valuable advice and helpful suggestions played an important role in completion of this work.

It is with profound sense of gratitude and regards that I express my thanks to Dr.(Mrs.) Sunita Arora, M.S., Associate Professor, Department of Obstetrics and Gynaecology, M.L.B. Medical College, Jhansi, under whose kind and worthy guidance and supervision I had the opportunity to carry out this work. To me she has been not only a source of encouragement and symbol of zest but also an unforgettable personality. The present work bears at every stage the impression of her keen interest in the progress of this work.

I am deeply indebted to Prof. R.C. Arora, M.D., D.Sc, Head, Department of Medicine, M.L.B. Medical College, Jhansi whose able guidance, constructive and valuable suggestions, reasoned criticism, devotion of previous time, meticulous attention to each and every details have gone a long way towards the success of this work.

I owe deep and heartful thanks to Dr. Navnit Agarwal, M.D., Assistant Professor, in Medicine for his patience in the elucidating the various aspects of the work carried in this department.

I am also thankful to faculty members of department of Obstetrics and Gynaecology - Dr.(Mrs.) Usha Agarwal, M.S., Dr. (Mrs.) Sanjaya Sharma, M.D., and Dr. (Mrs.) Sushila Kharkwal, M.D. for their constant encouragement and guidance throughout the study.

I deeply value the mental and moral support of my colleagues throughout the study.

I also pay my thanks to Mr. Phool Chandra Sachan for the meticulous manner in which he has typed the script of this thesis. I offer my thanks to Mr. A.K. Tiwari for his expert laboratory assistance.

I bow in reference to my lady subjects who have formed the material for present study.

Finally I pay my regards and thanks to my parents, husband Dr. Kamal Purshottam and friend Dr. Sarika Srivastava. No success of mine is apart from my loving husband and it is to him I dedicate this work.

Dated :

Lovelesh Kumari

(Lovelesh Kumari)

I N T R O D U C T I O N

INTRODUCTION

India with a population of 843.93 million (1991) is the second most populous country in world with only 2.4% of world's land area. India is supporting 16% of the world's population. India's population is increasing at the rate of 16 million per year. If current annual growth rate of 2.4% continues unchecked, the population of India at the turn of century may well reach one billion.

The growing concern about the population explosion is equally increasing the problem of side effects by the means to control it. The contraceptive methods may be broadly grouped into two classes.

I. SPACING METHOD

a. Barrier method
   i) Physical
   ii) Chemical
   iii) Combined methods

b. Intrauterine devices.

c. Hormonal methods and non hormonal oral contraceptive pills, hormonal injectible, implantable methods.

d. Post conception method.

II. TERMINAL METHODS

a. Male sterilization.

b. Female sterilization.

Progesterone was postulated by Beard (1897) and isolated in 1934. Pinous (1956) reported that daily doses of 300 mg of progesterone may inhibit ovulation in women but that control of ovulation was not regularly achieved, probably because of variable absorption from GI tract.

Ironically the progestin that was first produced norethynodrel is converted by the body to an estrogen so that the first progestational agent actually had both strong progestational and estrogenic effects.

The first successful clinical trial of a combined oral contraceptive pills were launched in Puerto Rico by Pincus and Rock et al (1956), called Enovid (10 mg tab) a combination of 10 mg norethynodrel and 150 microgram mestranol.

Since 1960, there has been definite trend towards prescribing lower doses of both the estrogen and progestin in pills. The field of oral contraception developed further as lower doses of Enovid was found to be effective; the 5 mg tablet has been approved for use in 1961.

In 1952 a second oral contraceptive orthonovum a combination of norethendrone and mestranol was approved.

Since 1960 approximately 37 different preparations have appeared. But none of them was free of side effects which were dose and age related, were nausea, vomiting, depression, breakthrough bleeding, amenorrhoea, weight gain,

hypertension, thromboembolism, thrombophlebitis, endometrial hyperplasia, coronary artery disease, due to alteration of lipid metabolism and increased incidence of acceleration of growth of pre-existing malignant lesion in breast cervix, liver endometrium.

The logical approach therefore was to develop need based agent that would not disturbb pituitary or ovarian functions but preventing pregnancy by interferring with preimplantation events. The knowledge that a critical balance between estrogen and progesterone is essential for development of fertilised ovum and preparation of uterus for implantation was utilised to develop the envisaged contraceptive.

Central drug research institute Lucknow and some centres in other cojntries including pharmaceutical industries designed and synthesized nonsteroidal estrogen antagonist with weak estrogenic activity aimed to prevent pregnancy by disturbing the delicate balance between estrogen and progesterone at uterine level but without interferring with their synthesis or blood levels.

Centchroman is outcome of these efforts which represent a major international breakthrough in contraceptive development.

Centchroman is a novel nonsteroidal moiety unrelated to any clinically used contraceptive and hence possesses no danger of cross sensitivity. Centchroman exhibit unique combination of weak estrogenic and potent

antiestrogenic properties which do not allow fertilised ovum to be implanted on endometrium thus avoiding pregnancy (Kamboj et al, 1971). It does not have side effects like nausea, vomiting, weight gain, breakthrough bleeding. (Population report No. 8,(1990) has no effect of platelet functions and no adverse effects on lipid profile (Nityanand et al, 1988) and no risk of cancer (Margveritte White James, Mc Gregor, Drug therapy, 1991).

More than two dozen oral steroid contraceptive preparations are currently marketed in world market. The majority of modification of first generation combined estrogen/pro-gesterone formulation. The second generation or sequential pills was used clinically for approximately a decade it was removed from market in 1976 due to its lower efficacy and possible association with endometrial carcinoma FDA Drug Bull, 1976). The third generation includes both the low dose combined estrogen progesterone pills (containing less than 50 microgram estrogen and less than 1.5 mg progesterone. They are among the most thoroughly studied drugs with over 25 new articles related to oral steroidal published each month.

While centchroman a new nonsteroidal oral contraceptive, although studies have shown that this is safe, effective drug in animals but has not been used extensively in human. Being nonsteroidal, non-hormonal there is high hope that it may be free from the most dreaded side effects

of hormonal pills i.e. IHD, and CVA mediated by their effect on lipoprotein coagulation and fibrinolysis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

RELATION OF LIPID LIPOPROTEIN PROFILE WITH MENSTRUAL CYCLE

Menstruation is periodic discharge of blood, mucus and cellular debris from the uterine mucosa and occurs at more or less regular cyclical and predictable interval from menarche to menopause except during pregnancy, lactation, anovulation, or pharmacological intervention.

Hormonal changes of cycle affects function of liver and so the lipid lipoprotein metabolism of body. There is 10-15% cyclic suppression of plasma total cholesterol, LDL and LDL apo beta during luteal phase while HDL increases during luteal phase of menstrual cycle (Kim and Kalkhaff et al, 1981).

RELATION OF LIPID LIPOPROTEIN PROFILE DURING PREGNANCY

During pregnancy total plasma triglyceride and cholesterol levels rise because of an increase in all lipoprotein including LDL, VLDL and HDL enriched in triglycerides. Increase of total apoprotein is caused by higher levels of VLDL apoprotein B. This hyperlipidaemia of pregnancy is attributed to derranged hepatic function during pregnancy (Svanberg and Vikrot, 1955; Aurell and Cramer, 1966).

EFFECT OF STEROIDAL CONTRACEPTIVES ON PITUITARY

Spellacy et al (1980) showed that oral contraceptives containing 50 microgram or more ethenyl estradiol suppress gonadotrophin release to a greater extent than the lower dose formulation. Mishell et al (1977) have provided evidence in humans that combined use of estrogens and progestins has a direct suppressive effect on pituitary gonadotrophins.

EFFECT OF CENTCHROMAN ON PITUITARY

Kamboj et al (1977) studied that centchroman (1.25 mg/kg for 7 days orally) had no effect on weight and total gonadotrophin content of the young male rat pituitary.

EFFECT OF STEROIDAL ORAL CONTRACEPTIVES ON OVARY

Maqueo et al (1972) studied that a large number of atretic follicles was seen when compared with ovaries from women not using contraceptives steroids. But this observation has not been confirmed in other studies by Starup et al. (1974).

EFFECT OF CENTCHROMAN ON OVARY

Kamboj et al (1977) studied that centchroman (0.25 mg/kg and 2.50 mg/kg) administered orally to immature female rats thrice daily for 3 days and there was no effect on their ovaries or their responsiveness

to exogenous ganadotrophins.

Singh et al (1982) gave centchroman even upto 10 times. The contraceptives dose to immature female rats and found no effect on ovaries or their responsiveness to exogenous gonadotrophins. In mated rats it has no effect on ovarian function even at 50 times the anti-implantation dose. Weekly doses of 120, 60 and 25 mg centchroman to women do not inhibit ovulation and show characteristic cyclic hormonal pattern. Thus, even at 4 times the contraceptive dose per week, centchroman does not suppress pituitary or ovarian function (Vaidya et al, 1977).

EFFECT OF ORAL STEROIDAL CONTRACEPTIVES ON UTERUS

Kar et al (1965) administered Enovid cyclically to prepubertal rhesus monkeys for period of 90 days to 3 years and observed an increase in uterine weight together with growth or serosa, muscularis and endometrium.

EFFECT OF CENTCHROMAN ON UTERUS

Oral administration of centchroman from 5-20 mg (total dose) in mice produced a linear increase in uterine weight. Similar dose related increase in uterine weight was also seen with ethenyl estradiol and mestranol. Simultaneous administration of oestrone and centchroman also cause in uterine weight but extent of uterotrophic response was less than that produced by oestrone alone (Kamboj et al, 1977).

EFFECT OF ORAL STEROIDAL CONTRACEPTIVES AND CENTCHROMAN ON VAGINA

Oral administration of centchroman in ovariectomized mice causes vaginal cornification which was 8 and 10 times less than that of mestranol and ethenyl estradiol respectively (Munshi, Nair and Devi, 1977).

EFFECT OF ORAL STEROIDAL CONTRACEPTIVES ON CERVIX

The sequential administration of estrogen and progestin induces a predecidual reaction together with considerable secretory activity of the cervical glands (Dunkin et al, 1963).

In 1967, Taylor et al reported on 13 patients who had a distinctive type of atypical polypoidal endocervical hyperplasia, among those 13 patients, 12 were taking oral steroidal contraceptives. Stern et al(1977) reported a prospective study of 300 women who had cervical dysplasia matched with 300 women who had normal cervical smears. The combined oral contraceptive pills chosen for the study contained 100 micro-gram mestranol and 1 mg ethynodiol diacetate. The patient with dysplasia who were taking oral contraceptives(compared with non users) showed a significantly increased conversion of dysplasia to carcinoma in situ after extended use (7 6 years).

EFFECT OF CENTCHROMAN ON CERVIX

Centchroman has no untoward effects on the cervix and uterus in women with cervical erosion or bulky uterus due to multiparity (Puri et al, 1988).

EFFECT OF STEROIDAL ORAL CONTRACEPTIVES ON BREASTS

Kahn et al (1965) postulated that norethynodral like other progestins stimulates the release of prolactin from pituitary.

The determination of deoxyribonucleic acid (DNA) has also been used as an index of mammary gland growth. Norethindrone did not increase the DNA content of the mammary gland and a combination of norethindrone with estradiol benzoate did not produce any effect greater than that of estradiol benzoate alone (Griffith et al, 1963).

The data from Royal College of General Practitioner study (1974) and the Walnat Greek contraceptive drug study (Ramcharan et al, 1974) suggested a slightly increased risk of breast cancer in women under 35 years of age with prolonged oral steroidal contraceptive use.

EFFECT OF CENTCHROMAN ON FOETUS

Oral administration of centchroman during the period of organogenesis to pregnant mice(25,50,100 mg/kg) and rabbits (20, 40, 80 mg/kg) did not have any deleterious effect either on mother or their litters. Histologically there was no evidence of any skeletal or visceral malformation in the foetuses (Sethi, 1977).

EFFECT OF STEROIDAL CONTRACEPTIVES ON FOETUS

Masculinization of female rats was obtained when the following progestins were administered during pregnancy : Norethindrone (Revesz et al, 1960), Norethynodral (Scholer et al, 1961), Medroxy progesterone acetate (Scholer et al, 1961).

ORAL HORMONAL CONTRACEPTIVES (COMBINED AND SEQUENTIAL) AND LIPID LIPOPROTEIN PROFILE

Lipoprotein metabolism is an important aspect of liver functions, which is apparently influenced by oestrogen progesterone treatment. Lipoproteins are classified according to their relative amount of lipid and proteins. LDL and VLDL can be described as carriers to peripheral tissues. HDL containing about 50% of protein are at present regarded as cholesterol regulators which transfer cholesterol from peripheral tissues including vascular epithelium to liver. HDL has also been suggested to block peripheral LDL receptors thereby reducing cholesterol uptake and storage in endothelial cells of vessels.

1. Serum Cholesterol

Wynn et al (1966) studied 102 women receiving oral contraceptive for more than 3 months and compared them with 75 normal females not taking any hormonal therapy. This study revealed an increase in serum cholesterol.

Faston et al (1970) studied effect of three

types of oral contraceptives having same constituents but in different amounts and found significant increase in group accepting high dose.

Wynn et al (1971) studied serum lipid levels in subjects using various combinations of contraceptive pills and found that sequential pills revealed least changes among the various pills studied.

Arora et al (1988) studied effect of sequential hormone on serum cholesterol in females of reproductive age group and found increase in serum cholesterol from 171.30 mg/dl to 192.34 mg/dl after 2 months of hormone use and to 213.45 mg/dl after 3 months of use.

2. Serum Triglycerides

Faston (1970) studied effect of dependent dose regimen of oral contraceptives on serum lipid levels and found significant rise in serum triglyceride levels in females using combined pills but no change with progestin only pills. In combined pills there was continuous rise but with progestin only pills there was a decrease after 3 months of oral contraceptive use in triglyceride levels and remain static for 2 years.

Wynn et al (1979) studied effect of various oral contraceptive pills containing doses of ethenyl oestradiol from 30 microgram to 150 microgram and revealed a dose related rise in triglyceride which was greatest in high dose oestrogen.

Krause et al (1983) found significant change in triglyceride levels 55 and 65 mg/dl for control and test groups respectively taking EE/NG (30 microgram/0.3 mg).

Arora et al (1988) found a significant rise in serum triglycerides levels in females using sequential hormones for 3 months.

3. High Density Lipoproteins (HDL)

Aurell and Cramer (1966) found a significant fall in serum HDL levels with use of oral contraceptives. Values fell from 60 to 46 mg/dl in test group.

Krause et al (1977) found that change in HDL depends upon relative amount of oestrogen and progestin. Progestin component is known to counter the effect of oestrogen on HDL level.

Krause et al (1983) compared two low dose oral pills in relation to lipid subclasses and found no change with norgestral group while significant change with norethindrone group.

Arora et al (1988) found that there was significant fall in levels of serum HDL in women using sequential hormones.

Estrogen usage alone increased the mean HDL levels approximately 10-20 mg/dl with EE_2, 20 microgram or 50 microgram increased HDL to a greater extent than daily conjugated estrogen 0.625 ng or 1.25 ng. Progestrogen only preparations, decrease mean HDL cholesterol concentration approximately 7-15 mg/dl and this occurs with both

17-acetoxy progesterone derivatives as well as the 19-nor-testosterone products. There is direct relationship between the dose of progestin and the reduction of HDL cholesterol (Bradley, Wingard and Petitti et al, 1978).

Briggs (1979) found almost all combinations products to decrease HDL cholesterol somewhat with 30 micro-gram EE_2 product, those pills with 0.5 mg norethindrone had minimal effect on mean HDL cholesterol while doubling the dose of protestogen to 1 mg norethindrone decreased mean HDL by 7 mg/dl (Levy and Feinleib, 1975).

The estrogen in a combined pill appears to decrease the serum concentration of low density lipoprotein, to increase high density lipoprotein but some progestine cause the reverse (Stadel, 1981). Almost certainly, the adverse changes noted in HDL; LDL ratios are the consequences of the 19-nortesto-sterone progestins and these changes are likely related to the specific progestin and its dose (Kauppinen-Makelin and colleagues, 1992). Importantly progestins can change the relative amount of total HDL, HDL_2 and HDL_3 (Tikanen and associates, 1981; 1982). It is believed that that the HDL_2 fraction provides cardiovascular protection (Miller and cc-workers, 1982). Therefore the estrogen and progestin effects the specific HDL_2 fraction are of special importance because oral contraceptive may alter a women's cardiovascular risk even though total HDL cholesterol values are unchanged. Briggs (1982) reported no change in total

HDL with levonorgestrel use, but Hatcher and colleagues (1990) found that it decreased HDL_2 and increased HDL_3. Apparently norethindrone containing oral contraceptives do not alter HDL_2 fractions (Hatches and associates, 1990; Krause and colleagues, 1983). More recently, however, Patsch and co-workers (1989) reported that two triphasic formulations containing norethindrone and one containing levonorgestrel, all had similar effects on total HDL, HDL_2 and LDL.

4. Serum LDL and VLDL

Krause et al (1983) foundthat VLDL increased with only noregestrel. LDL was significantly lower in norethesterone group.

Arora et al (1988) observed significant rise in serum LDL and VLDL levels in females of reproductive age group using sequential pills for 3 months.

5. Centchroman and its effect on lipid levels

Nityanand et al (1988) studied 122 women taking centchroman for more than one year, there was no change in serum lipid profile as compared to control subjects.

AIMS AND OBJECTIVES

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To evaluate :-

1. Acceptability, safety, efficacy and adverse drug reaction.

2. Changes in lipoprotein profile of females of reproductive age group using different oral contraceptives :
   i) Combined pills - viz. Mala-N.
   ii) Triphasic pills - viz. Orthonovum 7.7.7
   iii) Nonsteroidal pills - viz. Centchroman.

MATERIAL AND METHODS

MATERIAL AND METHODS

Present study was carried out in the departments of Obstetrics & Gynaecology and Medicine, M.L.B. Medical College, Hospital, Jhansi in a period of 12 months.

SELECTION OF CASES

313 women of reproductive age group were studied initially. Out of them 125 women were selected for trial. Out of these 125 women, 100 were put in study group and remaining 25 were taken as control group. From study group 20 women dropped out due to their personal reasons.

Inclusion Criteria

1. Volunteers were having normal menstrual cycle.
2. Post abortion cases were enrolled after at least one normal cycle.

Exclusion Criteria

1. Females with liver disease, ischaemic heart disease, hypertension, hyperlipidemia, diabetes, renal disease, acute or recurrent vascular thrombosis were not included in the study.
2. Females who were taking hormones prior to commencement of oral contraceptives, were also excluded from the study.

3. Females, whose basal endometrial histology showed evidence of endometrial hyperplasia and adenocarcinoma, were excluded from the study.
4. Females on drugs that are liable to interfere with lipid metabolism and thereby influencing lipoprotein levels in blood, were not considered for the study.

All the subjects received verbal and written information about the trial and gave their consent in writing. Detailed history of preset, past illness, family history, obstetric and menstrual history, dietary history, history of intake of any hormonal preparation prior to commencement of therapy.

A complete general and systemic examination including pelvic examination with special reference to height, weight and blood pressure were done in each case.

All the subjects were of average built. They were divided into 3 groups depending upon type of oral contraceptive pills they used.

Group A : Women using Mala-N (combined pills).
Group B : Women using Orthonovum 7.7.7 (sequential pills).
Group C : Women using Centchroman (nonsteroidal pills).

Following investigations were performed in all the cases.

ROUTINE

Haemoglobin, blood urea, blood sugar, urine albumin and sugar were done in each case.

SPECIAL

Serum total cholesterol, serum triglycerides, serum low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL), liver function test, platelet function test were done.

METHOD OF COLLECTION OF BLOOD SAMPLES

5 ml of blood after 12-14 hour fasting was withdrawn after 10 minutes of rest and without producing venous stasis.

After withdrawal blood was allowed to settle down for ½ hour and then centrifuged and serum was preserved. Blood samples were collected at (1) first visit to hospital. (2) one month after hormone therapy/ Centchroman therapy. (3) two months after hormone/centchroman therapy. (4) Three months after hormone/centchroman therapy. (5) Six months after hormone/centchroman therapy. (6) Eight months after hormone/centchroman therapy. (7) Twelve months after hormone/centchroman therapy.

Dosage Schedule

Combined pills : Mala-N supplied by Govt of India containing Ethenyl oestradiol - 0.03 mg and Norethesterone acetate - 1 mg.

Sequential pills : Orthonovum-7.7.7

7 tabs. - 0.05 mg norethesterone acetate+35 microgram EE.
7 yabs. - 0.75 mg " " + " " "
7 tabs. - 1.00 mg " " + " " "

Centchroman : 30 mg tab oral twice a week for first 3 months and then once a week schedule. Treatment was started from 1st day of menses. From 4th month onwards females were instructed to take one tablet on every Sunday irrespective of menses day.

ESTIMATION OF LIPID FRACTIONS

Various lipid fractions : serum total cholesterol (STC), serum triglycerides (STG), high density lipoproteins (HDL), were estimated by diagnostic chemical kits while low density lipoproteins (LDL) and very low density lipoproteins (VLDL) and LDL/HDL ratio were derived from above mentioned values by standard formulae.

1. STC

STC was estimated by commercial kits supplied by Ethnor. The basic principles is that cholesterol reacts with list solution of ferric perchlorate, ethyl acetate and sulphuric acid and gives a lavender coloured complex which is measured colorimetrically.

2. STG

Serum triglycerides was estimated by acetyl acetone method. Principle behind is that triglycerides are determined by measuring glycerol after its liberation from fatty acid by saponification. Glycerol is oxidised or by sodium metaperiodate to formaldehyde which is directly proportional to the amount of triglycerides.

3. HDL

HDL was estimated by utilizing commercial kits supplied by Ethnor. Basic principle is that the HDL cholesterol fraction is separated by using a precipitating reagent. The precipitate contains chylomicrons, VLDL, LDL, which are removed by centrifugation. The supernatant contains HDL cholesterol which is estimated by HDL-c colour reagent which gives purple coloured complex which is measured colorimetrically at 560 nm. The intensity of colour developed is proportional to the concentration of HDL-c in the specimen under test.

4. VLDL

VLDL is estimated by formula given by Friedwald et al (1972). This formula is valid upto STG values to less than 400 mg/dl.

VLDL (mg/dl) = STG/5.

5. LDL

LDL was calculated by the following formula given by Fredrickson DA (1972) :

LDL (mg/dl) = STC - (STG/5 + HDL) OR

LDL (mg/dl) = STC - (VLDL + HDL)

6. LDL:HDL Ratio

Statistical method used : Student 't' test was applied in the statistical analysis to compare the mean values of different groups.

OBSERVATIONS

OBSERVATIONS

In the present study we have evaluated acceptability, safety, efficacy, adverse drug reaction and changes in lipoprotein profile of females of reproductive age group using different oral contraceptives.

Initially 321 women were studied. Out of them 125 were selected for the trial. Out of these 125, 25 were taken as controls means women who were not taking any type of hormonal therapy and 100 women were taken as subjects and they were further divided into 3 groups according to the type of oral contraceptives, they were advised to take. From these 100 women 20 women dropped out in the initial phase of study due to their personal reasons.

TABLE I : Distribution of women in 4 groups.

Group	Type of oral contraceptive used	No.of cases	Percentage	Mean age (yrs.)	Mean weight (kgs)	Parity
A	Mala-N(Combined pills)	20	19.05	26.95 ±5.11	51.90 ±3.44	0-3
B	Orthonovum 7-7-7 (Triphasic pills)	20	19.05	26.25 ±5.39	50.95 ±3.50	0-3
C	Centchroman (Non steroidal)	40	38.10	25.92 ±4.55	52.27 ±4.00	0-3
D	Control subjects not taking any hormonal therapy	25	23.80	29.72 ±6.57	52.56 ±3.02	0-4

Out of 80 cases, 20 cases from group C, 6 from group A, 6 from group B came for regular follow up for 12

months. 12 females from group C and 8 cases from group A and B each came for regular follow up for initial 6 months. Six cases each from group A and B and 8 cases from group C came for an irregular follow up for initial 6 months although they have taken the pills regularly.

DIVISION OF GROUPS INTO SUBGROUPS

Group A, B, and C were further divided into following subgroups :

Group a : Females with regular follow up for 12 months.

Group b : Females with regular follow up for 6 months.

Group C : Females with an irregular follow up for 6 months.

No further division was done in group D. All the females of this group came for regular check up for 12 months at 3 monthly interval.

TABLE II : Distribution of females in subgroups.

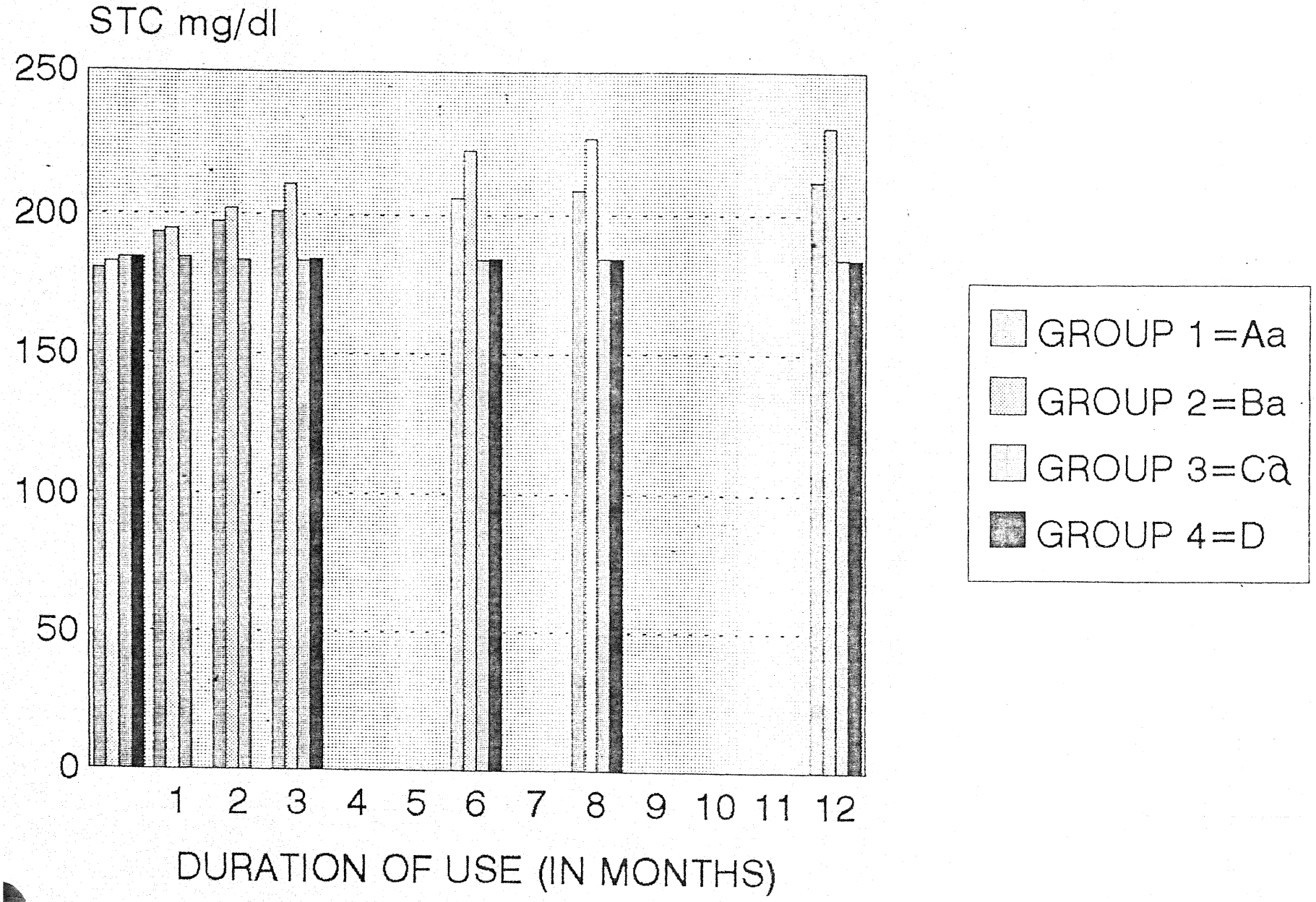
Group	Subgroups		
	a	b	c
A	6	8	6
B	6	8	6
C	20	12	8

Observed results of these cases are mentioned in various table forms.

Abbreviations used in various tables and master chart are as follows :

STC : Serum total cholesterol.

STG : Serum triglycerides.


STC mg/dl
250
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10 11 12
DURATION OF USE (IN MONTHS)
GROUP 1=Aa
GROUP 2=Ba
GROUP 3=Ca
GROUP 4=D

HDL : Serum high density lipoproteins.

LDL : Serum low density lipoproteins.

Wt. : Weight (kgs.)

Ht. : Height (Inches)

't' value was calculated by using Paired 't' test :

$$t = \frac{\bar{X} \sqrt{N}}{S}$$

where : $\bar{X}$ is the difference of means.

N is number and

S is standard deviation.

TABLE III : Oral contraceptive pills and STC.

Groups	STC mg/dl (Mean±S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	180.33 ± 6.25	193.16 ±11.99	197.16 ±11.90	201.16 ±10.20	206.16 ± 9.38	208.83 ±10.32	212.16 ±10.08
Ba (n=6)	182.83 ± 5.67	194.66 ±7.89	202.16 ± 8.01	210.83 ± 6.99	222.66 ± 5.75	226.66 ± 6.65	230.50 ± 5.24
Ca (n=20)	184.55 ± 3.61	184.55 ± 3.67	183.55 ± 3.72	183.45 ± 3.56	183.75 ± 3.22	184.20 ± 3.44	184.40 ± 3.37
D (n=25)	184.64 ± 7.37	-	-	184.28 ± 7.54	184.28 ± 6.77	184.00 ± 7.50	184.24 ± 7.55

Table III shows the effect of combined pills, triphasic pills and centchroman on serum total cholesterol in group Aa, Ba, Ca and their comparison with control group D.

Significant values are given below :

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 1	4.75	<0.01	0 Vs 2	6.06	<0.01
0 Vs 3	11.15	<0.001	0 Vs 6	16.12	<0.001
0 Vs 8	13.70	<0.001	0 Vs 12	26.64	<0.001
Group Ba					
0 Vs 1	8.45	<0.001	0 Vs 2	9.17	<0.001
0 Vs 3	11.08	<0.001	0 Vs 6	16.03	<0.001
0 Vs 8	17.40	<0.001	0 Vs 12	23.54	<0.001

TABLE IV : Oral contraceptive pills and STC.

Groups	STC mg/dl (Mean ± S.D.)				
	Month 0	1	2	3	6
Ab (n=8)	175.87 ± 8.99	182.00 ± 8.21	190.12 ± 8.42	198.25 ± 6.11	201.50 ± 5.37
Bb (n=8)	175.60 ± 9.95	180.25 ± 9.25	188.62 ± 9.39	196.12 ± 9.89	207.50 ± 5.92
Cb (n=12)	185.66 ± 5.33	185.41 ± 4.71	185.66 ± 4.63	185.91 ± 4.62	186.08 ± 4.35

Table IV shows the effect of combined pills, triphasic pills and centchroman on STC in group Ab, Bb and Cb.

Significant values are given below :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 1	9.21	<0.001	0 Vs 2	13.00	<0.001
0 Vs 3	1391	<0.001	0 Vs 6	15.20	<0.001
Group Bb					
0 Vs 1	10.48	<0.001	0 Vs 2	16.33	<0.001
0 Vs 3	13.65	<0.001	0 Vs 6	11.50	<0.001

TABLE V : Oral contraceptive pills and STC.

Groups	STC mg/dl (Mean±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	180.83 ± 6.70	191.66 ±11.99	-	-	-	202.33 ±10.48	-
Bc (n=6)	180.66 ± 5.60	-	192.83 ±11.77			212.00 ± 5.76	
Cc (n=8)	184.87 ± 4.35	-	184.75 ± 4.62	-	184.50 ± 4.20	-	185.12 ± 5.13

Table V shows the effect of combined pills, triphasic pills and centchroman on STC in group Ac, Bc and Cc.

Significant values are given below.

Values	't'	'p'	Value	't'	'p'
Group Ac					
0 Vs 1	4.64	<0.01	0 Vs 5	12.10	<0.001
1 Vs 5	13.80	<0.001			
Group Bc					
0 Vs 2	4.58	<0.01	0 Vs 5	25.00	<0.001
2 Vs 5	7.11	<0.001			

It is evident from table III, IV and V that there is rise in levels of STC after after 1, 2, 3, 6, 8 and 12 months of use of oral contraceptive pills in group Aa, Ab, Ac, Ba, Bb and Bc while the rise in STC was not statistically significant in group Ca, Cb, Cc and D.

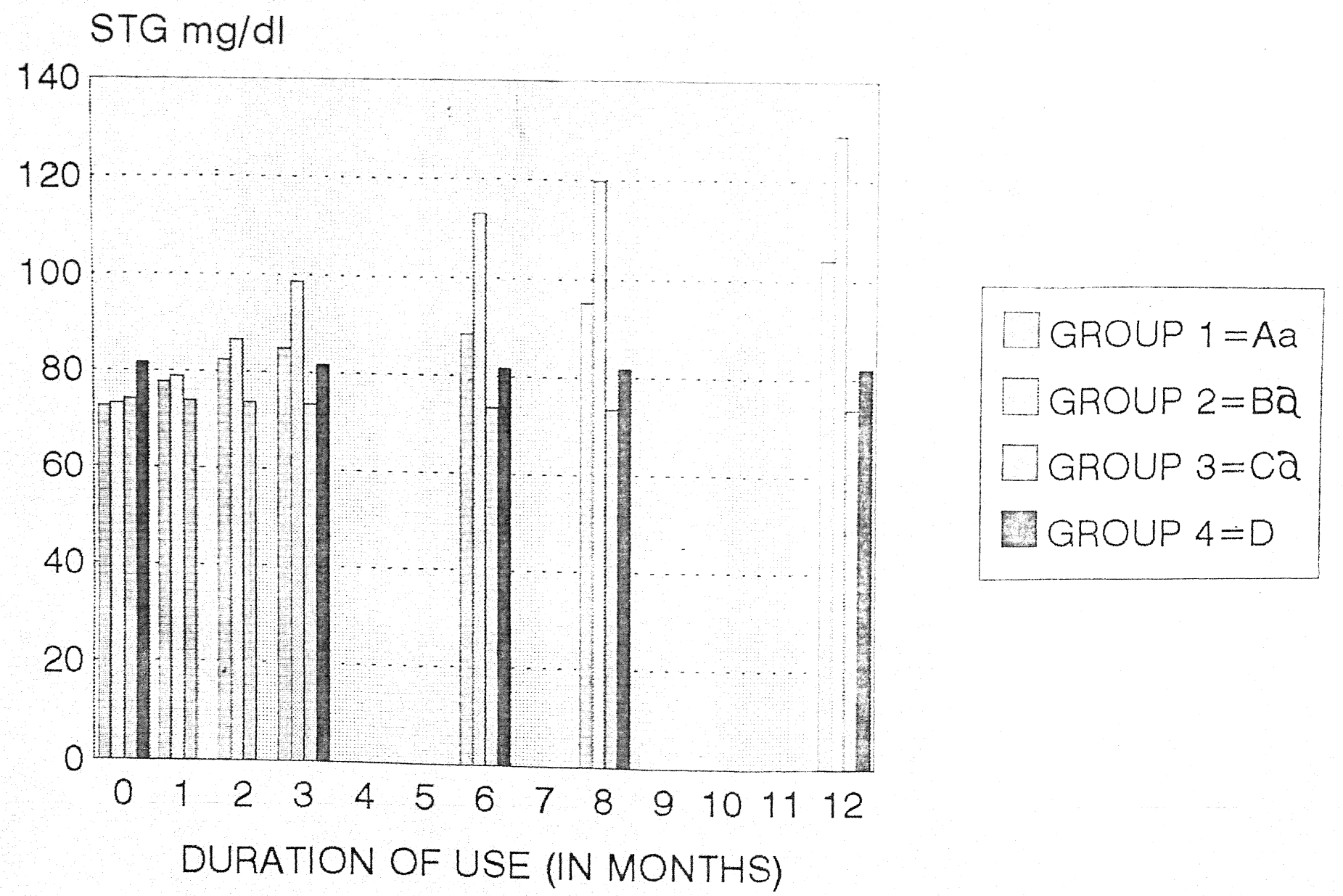
So it can be said that there was rise in STC started even after 1 month use of combined or triphasic pills. While there is no rise in STC in females using centchroman even after 12 month of use.

In group A and B there was gradual rise in STC although the levels were within the normal range, none of female of group A and B showed hypercholesterolemia.

The mean rise in STC in females of group Aa after 6 months use of Mala-N was 16 mg/dl from basal levels and after 12 months the mean rise was 26 mg/dl.

COMPARATIVE EFFECT OF CENTCHROMAN VS HORMONAL CONTRACEPTIVE PILLS ON SERUM TRIGLYCERIDES (STG)

STG



In group Ba after 6 months of use of Orthonovum 7-7-7 the mean rise in STC was 39.8 mg/dl, after 12 months 47.66 mg/dl from the basal levels.

So although there was rise in STC but it was more in group B, while there was no effect of centchroman on STC in group C.

TABLE VI : Oral contraceptive pills and STG.

Groups	STG mg/dl (Mean±S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	72.66 ± 2.58	77.83 ± 4.35	82.50 ± 3.39	85.00 ± 2.52	88.66 ± 3.07	95.33 ± 2.50	104.16 ± 1.72
Ba (n=6)	73.16 ± 4.57	78.83 ± 4.83	86.66 ± 5.31	98.66 ± 4.63	113.00 ± 6.13	119.83 ± 6.14	129.16 ± 6.27
Ca (n=20)	74.15 ±12.05	73.95 ±12.00	73.80 ±11.90	73.65 ±11.88	73.65 ±12.01	73.65 ±12.04	73.80 ±12.14
D (n=25)	81.68 ± 4.82	-	-	81.80 ± 5.47	81.76 ± 5.00	81.76 ± 4.70	81.92 ± 5.17

Table VI shows the effect of combined, triphasic pills and centchroman on STG in groups Aa, Ba, Ca and their comparison with control group D.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 2	24.57	<0.001	0 Vs 3	37.29	<0.001
0 Vs 6	25.45	<0.001	0 Vs 8	37.01	<0.001
0 Vs 12	29.90	<0.001			
Group Ba					
0 Vs 3	2.73	<0.05	0 Vs 6	3.25	<0.05
0 Vs 8	3.26	<0.05	0 Vs 12	6.16	<0.01
1 Vs 12	6.71	<0.01	2 Vs 12	6.82	<0.01

TABLE VII : Oral contraceptive pills and STG.

Groups	STG mg/dl (Mean±S.D.)				
	Month 0	1	2	3	6
Ab (n=8)	76.12 ± 6.19	83.62 ± 4.17	88.37 ± 3.92	95.12 ± 4.30	98.75 ± 4.39
Bb (n=8)	76.12 ± 6.19	84.62 ± 9.00	90.12 ± 7.43	97.00 ± 7.32	105.87 ± 7.23
Cb (n=12)	72.00 ± 9.19	72.66 ± 9.51	72.83 ± 8.83	72.33 ± 8.97	72.58 ± 8.98

Table VII shows the effect of combined pills, triphasic pills and centchroman on STG in group Ab, Bb and Cb.

Significant values are given below :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 1	3.65	<0.05	0 Vs 2	7.82	<0.001
0 Vs 3	15.5	<0.001	0 Vs 6	18.7	<0.001
Group Bb					
0 Vs 1	5.60	<0.001	0 Vs 2	16.23	<0.001
0 Vs 3	11.08	<0.001	0 Vs 6	16.09	<0.001

TABLE VIII : Oral contraceptive pills and STG.

Groups	STG mg/dl (Mean±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	79.00 ± 4.81	81.66 ± 4.76	-	-	-	88.66 ± 4.27	-
Bc (n=6)	73.33 ± 7.96	-	79.16 ± 8.08	-	-	88.00 ± 8.94	
Cc (n=8)	72.73 ± 6.73	-	73.12 ± 6.85	-	73.25 ± 6.79	-	73.37 ± 7.15

Table VIII shows the effect of combined pills, triphasic pills and centchroman on STG in group Ac, Bc and Cc.

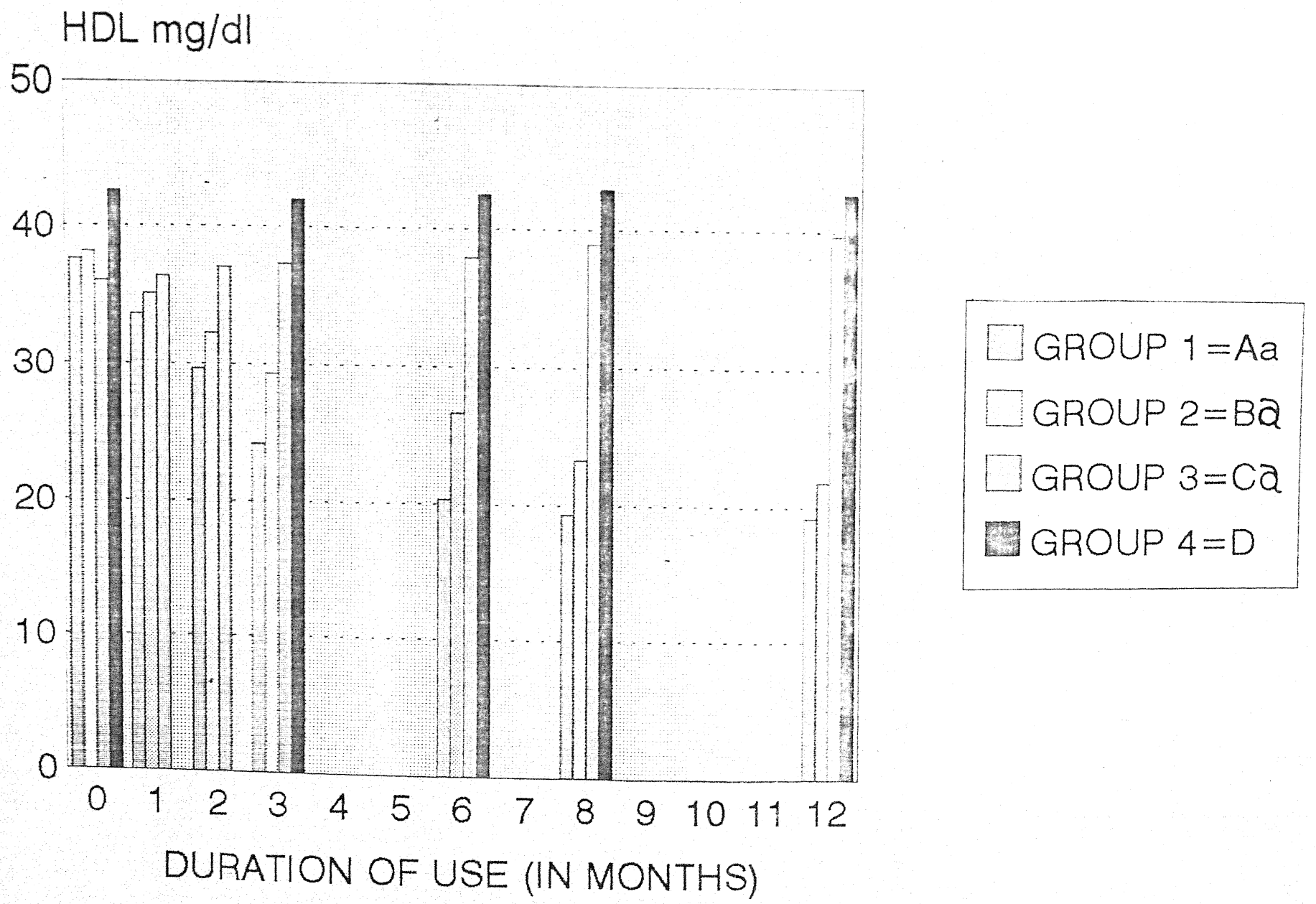
Significant values are given below :

Values	't'	'p'	Values	't'	'p'
Groups Ac					
0 Vs 1	8.04	<0.001	0 Vs 5	13.5	<0.001
1 Vs 5	13.6	<0.001			
Group Bc					
0 Vs 2	8.30	<0.001	0 Vs 5	6.76	<0.001
2 Vs 5	5.20	<0.001			

It is evident from table VI, VII and VIII that there was rise in levels of STG after 1,2,3, 6, 8 and 12 months use of combined pills and triphasic pills in group Aa, Ab, Ac, Ba, Bb and Bc while there was no rise in group Ca, Cb, Cc and D.

So it can be said that rise in STG was highly significant in females using combined and triphasic pills even after one month of use, while it was insignificant even after 12 month use of centchroman when the values were compared with basal values as well as with one month values.

Although none of the females of group A and B showed hypertriglyceridemia but there was a definite rising trend in levels of STG in females using hormonal contraceptives either Mala-N or Orthonovum 7-7-7. The mean rise in STG levels after 6 months of use of Mala-N in group Aa was 16 mg/dl after 12 months of use of Mala-N


HDL mg/dl
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12
DURATION OF USE (IN MONTHS)
GROUP 1 = Aa
GROUP 2 = Ba
GROUP 3 = Ca
GROUP 4 = D

31.5 mg/dl, after 6 months of use in group Ab 22.62 mg/dl.

In group Ba, after 6 month of use of orthonovum 7-7-7 the mean rise in STG was 39.8 mg/dl, after 12 month of use - 56 mg/dl. In group Bb after 6 months of use 29.75 mg/dl from basal levels.

In group C there was no effect on STG when compared with basal levels.

TABLE IX : Oral contraceptive pills and HDL.

Groups	HDL mg/dl (Mean ± S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	37.66 ± 1.86	33.66 ± 3.14	29.55 ± 1.63	24.16 ± 1.72	20.33 ± 2.06	19.33 ± 2.65	19.16 ± 2.13
Ba (n=6)	38.16 ± 4.70	35.16 ± 4.49	32.33 ± 3.44	29.33 ± 3.20	26.66 ± 3.14	23.33 ± 3.01	21.83 ± 1.94
Ca (n=20)	36.10 ± 2.90	36.45 ± 2.94	37.10 ± 2.86	37.40 ± 2.89	37.95 ± 3.21	39.00 ± 2.57	39.70 ± 2.40
D (n=25)	42.53 ± 5.62	-	-	41.92 ± 5.50	42.52 ± 6.25	42.92 ± 6.52	42.72 ± 6.32

Table IX shows the effect of combined pills, triphasic pills and centchroman on HDL in groups Aa, Ba, Ca and their comparison with control group D.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 1	3.65	<0.05	0 Vs 2	17.98	<0.001
0 Vs 3	21.90	<0.001	0 Vs 6	14.25	<0.001
0 Vs 8	11.32	<0.001	0 Vs 12	11.22	<0.001
Group Ba					
0 Vs 1	4.77	<0.01	0 Vs 2	5.95	<0.001
0 Vs 3	9.74	<0.001	0 Vs 6	10.59	<0.001
0 Vs 8	11.64	<0.001	0 Vs 12	11.08	<0.001

Group Ca					
0 Vs 1	3.57	∠0.01	0 Vs 2	8.94	∠0.001
0 Vs 3	12.51	∠0.001	0 Vs 6	7.10	∠0.001
0 Vs 8	8.05	∠0.001	0 Vs 12	10.31	∠0.001

TABLE X : Oral contraceptive pills and HDL.

Groups	HDL mg/dl (Mean ± S.D.)				
	Month 0	1	2	3	6
Ab (n=8)	50.12 ± 2.69	45.25 ± 3.65	43.37 ± 2.72	41.62 ± 2.77	33.75 ± 3.05
Bb (n=8)	31.37 ± 2.26	30.50 ± 1.85	28.25 ± 1.66	23.37 ± 2.87	18.87 ± 2.90
Cb (n=12)	31.83 ± 1.52	34.25 ± 1.86	37.83 ± 1.64	42.16 ± 1.33	42.83 ± 1.46

Table X shows the effect of combined pills, triphasic pills and centchroman on HDL in groups Ab, Bb and Cb.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 1	15.36	∠0.001	0 Vs 2	9.48	∠0.001
0 Vs 3	8.54	∠0.001	0 Vs 6	13.53	∠0.001
Group Bb					
0 Vs 1	3.01	∠0.05	0 Vs 2	5.63	∠0.001
0 Vs 3	10.01	∠0.001	0 Vs 6	15.65	∠0.001
Group Cb					
0 Vs 1	12.64	∠0.001	0 Vs 2	24.40	∠0.001
0 Vs 3	22.10	∠0.001	0 Vs 6	19.50	∠0.001

TABLE XI : Oral contraceptive pills and HDL.

Groups	HDL mg/dl (Mean±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	39.16 ± 4.26	34.33 ± 3.88	-	-	-	23.00 ± 3.74	-
Bc (n=6)	38.16 ± 2.78	-	32.83 ± 3.65	-	-	25.16 ± 5.34	-
Cc (n=8)	39.12 ± 2.94	-	41.12 ± 2.85	-	43.00 ± 2.82	-	43.37 ± 2.72

Table XI shows the effect of combined pills, triphasic pills and centchroman on HDL in groups Ac, Bc and Cc.

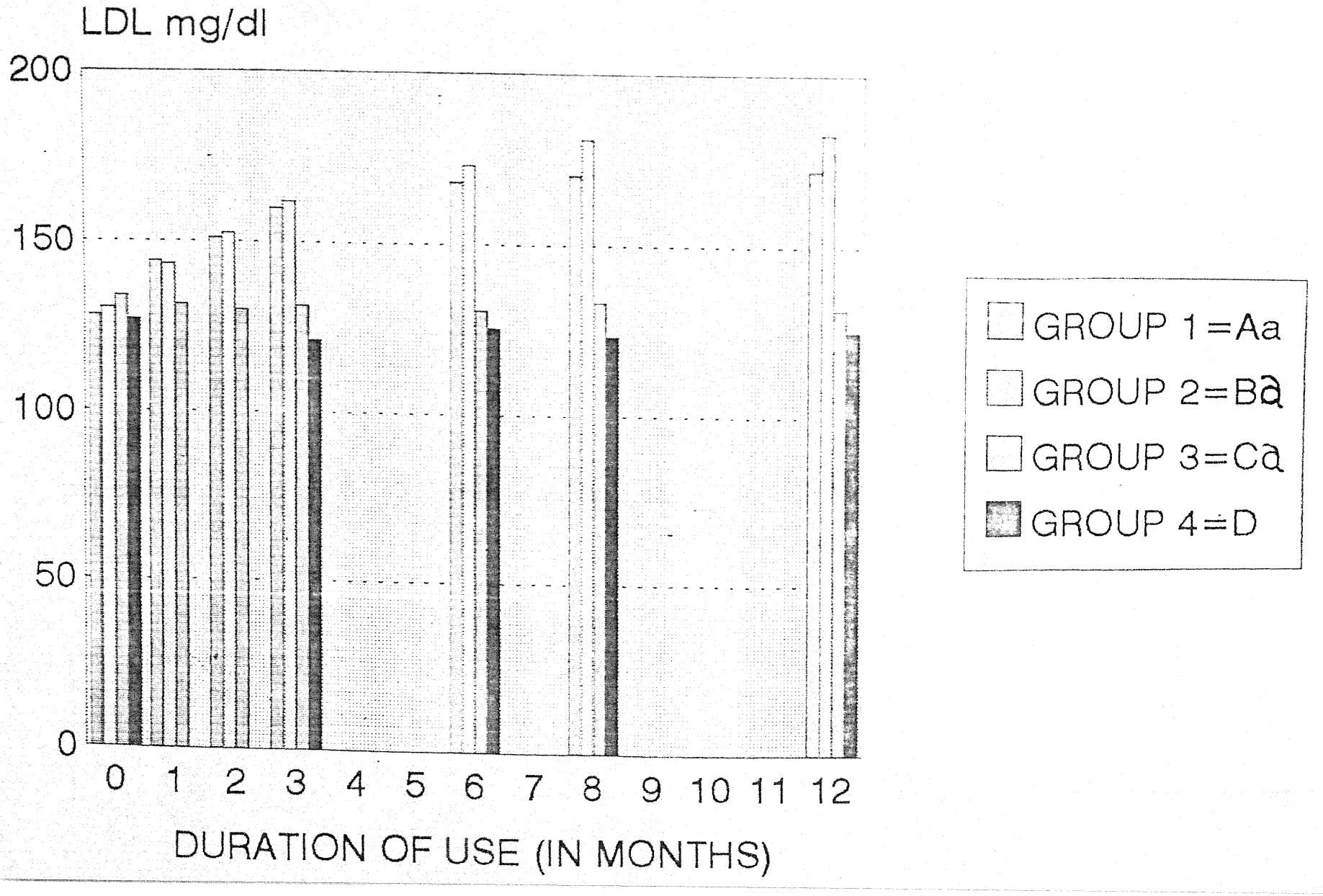
Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ac					
0 Vs 1	3.45	<0.05	0 Vs 5	24.74	<0.001
1 Vs 5	7.93	<0.001			
Group Bc					
0 Vs 2	9.60	<0.001	0 Vs 5	6.79	<0.001
2 Vs 5	4.39	<0.01			
Group Cc					
0 Vs 2	7.50	<0.001	0 Vs 4	8.11	<0.001
0 Vs 6	6.33	<0.001	2 Vs 4	4.26	<0.001

It is evident from Tables IX, X and XI that there was gradual decrease in HDL levels in females taking steroidal contraceptive pills either combined or triphasic while there was gradual increase in HDL infemales taking centchroman as compared with control subjects.

EFFECT OF CENTCHROMAN VS HORMONAL PILLS ON LOW DENSITY LIPOPROTEINS (LDL)

LDL



So it can be said that there was significant decrease in HDL levels in females taking combined and triphasic pills, while there was significant increase in HDL levels in females taking centchroman when the values were compared to their basal values and with control group.

The mean decrease in HDL levels in group Aa after 6 month use of Mala-N was 17.33 mg/dl, after 12 months use of Mala-N was 18.5 mg/dl and in group Ab decrease was 16.37 mg/dl after 6 months use of Mala-N.

In group Ba the mean decrease in HDL levels after 6 months use of Orthonovum 7-7-7 was 11.5 mg/dl, after 12 month use was 16.33 mg/dl. In group Bb mean decrease was 12.50 mg/dl in HDL after 6 months use of Orthonovum 7-7-7.

In group C after 6 months use of centchroman the mean rise in HDL levels was 2.21 mg/dl and after 12 months the rise was 3.6 mg/dl.

TABLE XII : Oral contraceptive pills and LDL.

Groups	LDL mg/dl (Mean ± S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	127.80 ± 4.83	144.00 ± 9.22	151.00 ±10.48	159.90 ± 8.75	168.10 ± 7.72	170.40 ± 8.19	172.10 ± 8.78
Ba (n=6)	130.03 ± 8.31	143.10 ± 8.34	152.50 ± 6.70	161.70 ± 6.73	173.06 ± 5.58	180.90 ± 6.20	182.80 ± 6.34
Ca (n=20)	133.62 ± 5.09	131.31 ± 5.50	129.99 ± 4.45	131.37 ± 4.68	130.67 ± 4.26	133.40 ± 4.47	131.69 ± 5.00
D (n=25)	126.68 ± 7.33	-	-	121.40 ±12.53	125.42 ± 4.28	123.74 ±10.03	125.22 ± 7.99

Table XII shows the effect of combined pills, triphasic pills and centchroman on LDL in groups Aa, Ba, Ca and their comparison with control group D.

Significant values are as follows:

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 1	7.28	<0.001	0 Vs 2	5.23	<0.001
0 Vs 3	16.21	<0.001	0 Vs 6	25.57	<0.001
0 Vs 8	23.36	<0.001	0 Vs 12	19.90	<0.001
Group Ba					
0 Vs 1	10.93	<0.001	0 Vs 2	8.03	<0.001
0 Vs 3	10.46	<0.001	0 Vs 6	13.76	<0.001
0 Vs 8	13113	<0.001	0 Vs 12	14.85	<0.001
Group Ca					
0 Vs 1	2.18	<0.05	0 Vs 2	4.57	<0.001
0 Vs 3	5.50	<0.001	0 Vs 6	6.57	<0.001
0 Vs 8	7.53	<0.001	0 Vs 12	8.35	<0.001

TABLE XIII : Oral contraceptive pills and LDL.

Groups	LDL mg/dl(Mean±S.D.)				
	Month 0	1	2	3	6
Ab (n=8)	126.90 ± 9.34	123.65 ± 9.05	129.07 ±10.60	134.00 ± 9.06	131.62 ± 7.42
Bb (n=8)	129.05 ± 9.39	132.90 ±10.45	142.35 ± 9.55	154.10 ± 9.49	167.45 ± 6.15
Cb (n=12)	139.40 ±06.04	136.80 ± 5.70	133.60 ± 5.02	130.10 ± 5.25	128.73 ± 5.36

Table XIII shows the effect of combined pills, triphasic pills and centchroman on LDL in groups Ab, Bb and Cb.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 2	3.09	<0.05	0 Vs 3	5.35	<0.01
0 Vs 6	3.91	<0.01			
Group Bb					
0 Vs 1	3.69	<0.001	0 Vs 2	15.37	<0.001
0 Vs 3	20.96	<0.001	0 Vs 6	23.88	<0.001
Group Cb					
0 Vs 1	5.69	<0.001	0 Vs 2	9.40	<0.001
0 Vs 3	13.40	<0.001	0 Vs 6	13.60	<0.001

TABLE XIV : Oral contraceptive pills and LDL.

Groups	LDL mg/dl (Mean±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	125.80 ± 5.89	141.00 ±13.86	-	-	-	161.60 ± 8.96	-
Bc (n=6)	127.80 ± 6.35	144.76 ±12.05	-	-	-	169.10 ± 8.94	-
Cc (n=8)	131.27 ± 5.97	-	129.00 ± 5.80	-	126.85 ± 5.49	-	127.07 ± 6.17

Table XIV shows the effect of combined pills, triphasic pills and centchroman on LDL in groups Ac, Bc and Cc.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Bc					
0 Vs 2	5.64	<0.01	0 Vs 5	10.30	<0.001
0 Vs 5	28.93	<0.001			
Group Cc					
0 Vs 2	4.76	<0.01	0 Vs 6	8.20	<0.001
0 Vs 8	5.91	<0.001			

It is clear from Table XII, XIII and XIV that there is gradual increase in serum LDL in females taking steroid oral contraceptives either Mala-N or Orthonovum 7-7-7, while in females taking centchroman there was light decrease in LDL levels when compared with basal LDL levels and with control subjects.

So it can be said that rise in LDL was highly significant in females taking hornomal oral contraceptive either Mala-N or Orthonovum 7-7-7 and this effect was observed from one month use of hormonal pills onwards, while in females taking centchroman, there was a significant decrease in LDL levels.

The mean rise in serum LDL in females after 6 month of use of Mala-N was 40.30 mg/dl in group Aa and after 12 months it was 43.70 mg/dl.

The mean rise in serum LDL in females after 6 months use of orthonovum 7-7-7 was 43.03 mg/dl, while after 12 months use of orthonovum 7-7-7was 52.8 mg/dl.

The mean decrease in serum LDL levels in females taking centchroman after 6 months of use was 10.7 mg/dl and after 12 months of use mg/dl.

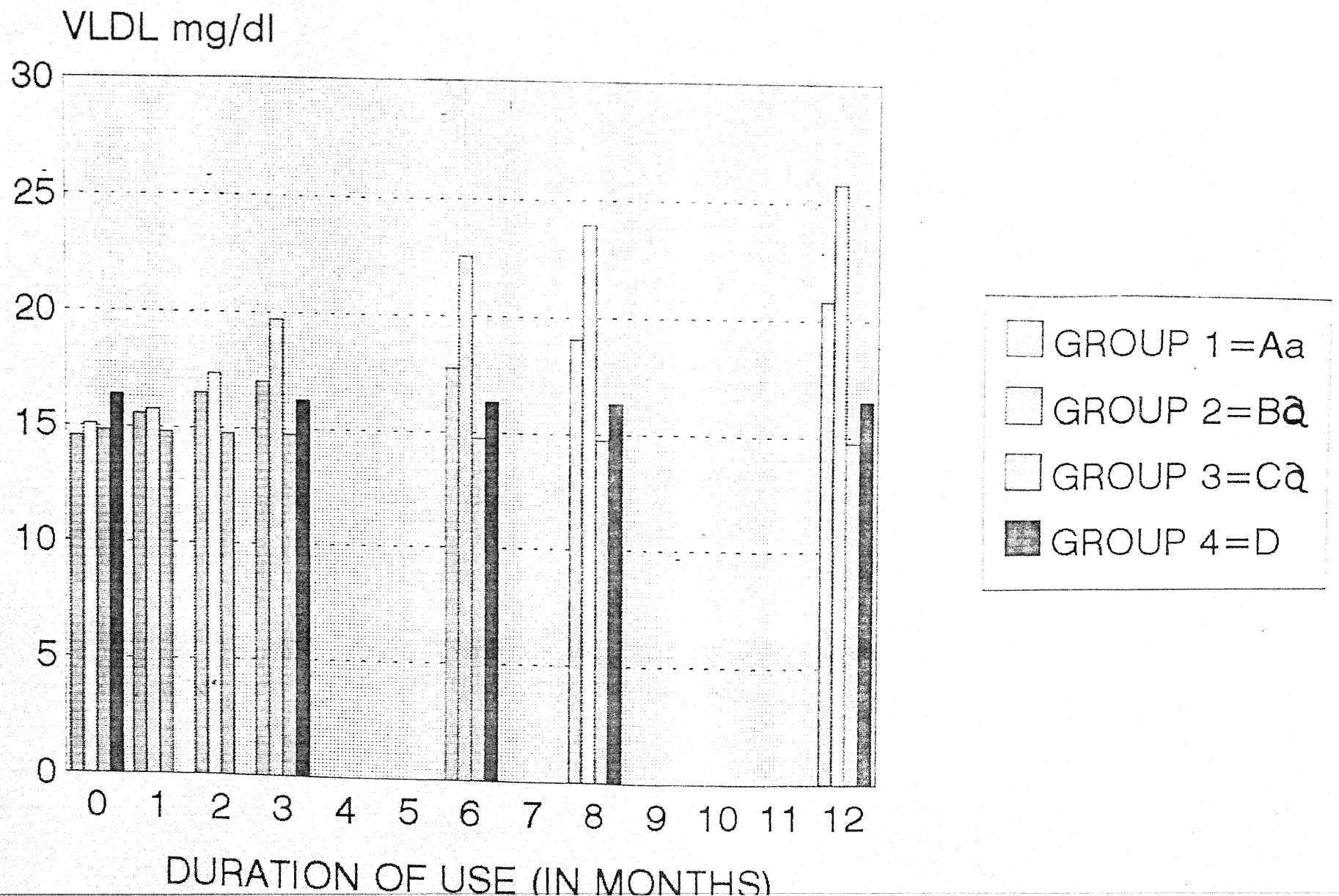

VLDL mg/dl
30
25
20
15
10
5
0
0 1 2 3 4 5 6 7 8 9 10 11 12
DURATION OF USE (IN MONTHS)
GROUP 1=Aa
GROUP 2=Ba
GROUP 3=Ca
GROUP 4=D

TABLE XV : Oral contraceptive pills and VLDL.

Groups	VLDL mg/dl (Mean±S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	14.53 ± 0.51	15.56 ± 0.87	16.50 ± 0.65	17.00 ± 0.50	017.73 ± 0.61	19.06 ± 0.50	20.83 ± 0.34
Ba (n=6)	15.06 ± 1.48	15.76 ± 0.96	17.33 ± 1.06	19.73 ± 0.92	22.60 ± 1.22	23.96 ± 1.22	25.83 ± 1.17
Ca (n=20)	14.83 ± 2.41	14.79 ± 2.40	14.76 ± 2.18	14.73 ± 2.37	14.73 ± 2.40	14.75 ± 2.43	14.76 ± 2.42
D (n=25)	16.37 ± 1.05	-	-	16.26 ± 1.04	16.34 ± 1.00	16.33 ± 0.92	16.52 ± 1.35

Table XV shows the effect of combined pills, triphasic pills and centchroman in groups Aa, Ba, Ca and their comparison with control group D.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 1	6.15	<0.01	0 Vs 2	25.20	<0.001
0 Vs 3	36.75	<0.001	0 Vs 6	26.10	<0.001
0 Vs 8	36.99	<0.001	0 Vs 12	30.26	<0.001
Group Ba					
0 Vs 1	13.80	<0.001	0 Vs 2	16.90	<0.001
0 Vs 3	24.60	<0.001	0 Vs 6	30.00	<0.001
0 Vs 8	35.16	<0.001	0 Vs 12	22.30	<0.001

TABLE XVI : Oral contraceptive pills and VLDL.

Groups	VLDL mg/dl (Mean±S.D.)				
	Month 0	1	2	3	6
Ab (n=8)	15.22 ± 1.23	16.72 ± 0.83	17.67 ± 0.78	19.00 ± 0.86	19.75 ± 0.87
Bb (n=8)	15.22 ± 1.48	16.92 ± 1.82	18.02 ± 1.48	19.40 ± 1.46	21.17 ± 1.44
Cb (n=12)	14.40 ± 1.83	14.53 ± 1.90	14.56 ± 1.76	14.46 ± 1.79	14.90 ± 1.79

Table XVI shows the effect of combined pills, triphasic pills and centchroman on VLDL in groups Ab, Bb and Cb

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 1	3.79	<0.01	0 Vs 2	7.87	<0.001
0 Vs 3	17.20	<0.001	0 Vs 6	18.81	<0.001
Group Bb					
0 Vs 2	8.35	<0.001	0 Vs 5	6.39	<0.01
0 Vs 5	4.98	<0.01			

TABLE XVII : Oral contraceptive pills and VLDL.

Groups	VLDL mg/dl (Mean±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	15.80 ± 0.96	16.33 ± 0.95	-	-	-	17.73 ± 0.85	-
Bc (n=6)	14.66 ± 1.59	-	15.83 ± 1.61	-	-	17.66 ± 1.91	-
Cc (n=8)	14.47 ± 1.34	-	14.62 ± 1.37	-	14.65 ± 1.35	-	14.66 ± 1.43

Table XVII shows the effect of combined pills, triphasic pills and centchroman on VLDL in groups Ac, Bc and Cc.

significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ac					
0 Vs 1	8.11	<0.001	0 Vs 5	13.60	<0.001
0 Vs 6	13.50	<0.001			

It is evident from Tables XV, XVI and XVII that there was gradual rise in serum VLDL in females taking steroidal oral contraceptives either combined or triphasic pills while in females taking centchroman there was no such effect seen when the levels were compared with basal values as well as with control group D.

So it can be said that in females using oral hormonal contraceptive either Mala-N or Orthonovum 7-7-7 there was gradual rise in serum VLDL levels. The mean rise in females of group A using Mala-N after 6 months use was 3.2 mg/dl, after 8 months of use it was 4.53 mg/dl and after 12 months of use was 6.3 mg/dl from basal values.

In group B after 6 months use of Orthonovum 7-7-7 mean rise in serum VLDL was 7.96 mg/dl, after 8 months use was 9.32 mg/dl, after 12 months use of Orthonovum 7-7-7 11.2 mg/dl for basal values.

In group C no significant changes in serum VLDL was observed in 12 months of use.

TABLE XVIII : Oral contraceptive pills and LDL/HDL.

Groups	LDL/HDL Ratio (Mean±S.D.)						
	Month 0	1	2	3	6	8	12
Aa (n=6)	3.39 ±0.16	4.12 ±0.50	5.00 ±0.36	6.63 ±0.46	8.31 ±0.75	8.92 ±1.02	9.05 ±0.90
Ba (n=6)	3.54 ±0.54	4.14 ±0.62	4.75 ±0.47	5.56 ±0.64	6.57 ±0.83	7.79 ±1.12	8.42 ±0.85
Ca (n=20)	3.71 ±0.38	3.68 ±0.41	3.56 ±0.40	3.55 ±0.32	3.43 ±0.32	3.32 ±0.33	3.30 ±0.23
D (n=25)	3.09 ±0.61	-	-	3.02 ±0.59	2.98 ±0.58	2.97 ±0.58	3.01 ±0.62

Table XVIII shows the effect of combined pills, triphasic pills and centchroman on LDL/HDL ratio in groups Aa, Ba and Ca and their comparison with control group D.

Significant values are given below :

Values	't'	'p'	Values	't'	'p'
Group Aa					
0 Vs 1	6.26	<0.01	0 Vs 2	15.36	<0.001
0 Vs 3	18.76	<0.001	0 Vs 6	13.94	<0.001
0 Vs 8	10.94	<0.001	0 Vs 12	15.44	<0.001
Group Ca					
0 Vs 1	3.50	<0.01	0 Vs 2	8.12	<0.001
0 Vs 3	7.69	<0.001	0 Vs 6	7.94	<0.001
0 Vs 8	8.94	<0.001	0 Vs 12	7.22	<0.001

TABLE XIX : Oral contraceptive pills and LDL/HDL.

Groups	LDL/HDL ratio (Mean±S.D.				
	Month 0	1	2	3	6
Ab (n=8)	3.78 ±0.47	2.95 ±0.37	2.99 ±0.40	2.98 ±0.43	2.63 ±0.26
Bb (n=8)	4.11 ±0.27	4.73 ±1.18	5.04 ±0.31	6.62 ±0.74	9.04 ±1.40
Cb (n=12)	4.38 ±0.28	4.00 ±0.29	3.49 ±0.29	3.08 ±0.18	3.00 ±0.17

Table XIX shows the effect of combined pills, triphasic pills and centchroman on LDL/HDL ratio in groups Ab, Bb and Cb.

Significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ab					
0 Vs 1	9.43	<0.001	0 Vs 2	6.58	<0.001
0 Vs 3	6.66	<0.001	0 Vs 6	9.59	<0.001

Group Bb					
0 Vs 1	2.59	∠0.05	0 Vs 2	9.60	∠0.001
0 Vs 3	10.07	∠0.001	0 Vs 6	10.68	∠0.001
Group Cb					
0 Vs 1	7.57	∠0.001	0 Vs 2	24.50	∠0.001
0 Vs 3	17.32	∠0.001	0 Vs 6	18.35	∠0.001

TABLE XX : Oral contraceptive pills and LDL/HDL ratio.

Groups	LDL/HDL ratio (Mean ±S.D.)						
	Month 0	1	2	3	4	5	6
Ac (n=6)	3.24 ±0.32	4.15 ±0.70	-	-	-	7.16 ±1.17	-
Bc (n=6)	3.36 ±0.32	-	6.43 ±0.61	-	-	7.00 ±1.73	
Cc (n=8)	3.37 ±0.37	-	3.16 ±0.30	-	2.96 ±0.28	-	2.94 ±0.28

Table XX shows the effect of combined pills, triphasic pills and centchroman on LDL/HDL ratio in groups Ac, Bc and Cc.

significant values are as follows :

Values	't'	'p'	Values	't'	'p'
Group Ac					
0 Vs 1	3.86	∠0.05	0 Vs 5	11.97	∠0.001
1 Vs 5	6.71	∠0.01			
Group Bc					
0 Vs 2	7.24	∠0.001	0 Vs 5	5.57	∠0.01
2 Vs 5	4.81	∠0.01			
Group Cc					
0 Vs 2	5.88	∠0.01	0 Vs 4	7.24	∠0.001
0 Vs 6	5.80	∠0.01	2 Vs 6	3.38	∠0.05

It is evident from Tables XVIII, XIX and XX that there was gradual but definite increase in LDL/HDL ratio in females of group A and B taking Mala-N and Orthonovum 7-7-7 respectively. While there was slight decrease in LDL/HDL ratio in females of group C taking centchroman. There was no significant change in females of control group.

So it can be said that rise in LDL/HDL ratio was highly significant in females using Mala-N and orthonovum 7-7-7 while there is significant decrease in LDL/HDL ratio in females using centchroman when the values were compared with basal values.

The mean rise in LDL/HDL ratio after 6 months use of Mala-N was 4.92 after 8 months use of Mala-N was 5.52 and after 12 months use of Mala-N it was 5.65.

In group B, after 6 months use of orthonovum 7-7-7 the mean rise in LDL/HDL ratio was 2.97, after 8 months was 4.30 and after 12 months it was 4.93.

In group C after 6 months use of centchroman mean fall in LDL/HDL ratio was 0.32 from basal levels. After 8 months use the mean fall was 0.40 and after 12 months use of centchroman the mean fall in LDL/HDL ratio was 0.42 from basal values.

TABLE XXI : Side effects observed in females of groups A, B and C taking combined pills, triphasic pills and centchroman respectively.

Side Effects	Group A (n=20)	Group B (n=20)	Group C (n=40)
Method failure	-	-	2
Nausea	6	8	-
Vomiting	2	2	-
Breakthrough bleeding	8	5	-
Prolonged cycle	-	-	10
Scanty menses	1	1	2
Weight gain	2	3	-
Depression	2	1	-
Decreased libido	2	1	-
Acne	2	1	-
Cholasma	1	-	-
Cervical hypertrophy	-	-	2
Breast dyscomfort	1	1	-
Ovarian enlargement	1	-	-

It is evident from Table XXI that nausea, and vomiting are more common side effects in females of group A and B while none of the female of group C complained about it. In group A and B, nausea and vomitings were more common during initial months of usage of pills. This side effect reduced when they advised to take the pills after meal and at bed time.

Breakthrough bleeding was the commonest side effect observed in females of group A (40% cases) and of group B (25% cases). The intermenstrual bleeding mainly in first half of cycle was observed during initial 3 months. The cycles became regular after 3 months moreovers females advised to take the pills at fixed time daily to overcome this side effect.

Prolonged cycles were observed in 25% females of group G ranging from 35-50 days. They were advised to get the pregnancy test done when the cycles were found to be of more than 40 days. They ressumed about it and cycles were almost normal of 30 days duration. When the continued with the drug for 3 months. In 5% cases pregnancy test was positive. Their ultrasound examination was carried out for foetal well being and the foetuses were absolutely normal. Out of these two cases one get pregnant during initial 2 months of centchroman therapy because she was not using any additional contraceptive method while other women get pregnant after 6 months of centchroman therapy although she was taking the drug regularly.

2(5%) cases of group C complained of mucoid discharge per vaginum on P/S examination their cervix hypertrophies but after antibiotics therapy they recovered after 2 weeks.

10% of group A and 15% females of group B gained weight. The mean gain in body weight was 5 kg after 12 months. In group B the females experienced increase in appetite.

10% females of group A and 5% females of group B experienced depression, lethargy, irritability and decreased libido.

10% females of group A and 5% females of group B developed acne unrelated to the menstrual cycle.

One (5%) case of group A developed butterfly rashes over face (chloasma). There was past history of same type rashes over face during her past 2 pregnancies. The rashes were gradually used to fade after 3 months postpartum.

One (5%) case of group A developed hypertension after 6 months use of combined pills. She was 30 years old weighing 60 kg. There was positive family history of hypertension. She was para 3 and there was no history of pre-eclamptic toxaemia during any of her pregnancy.

The overall observations of our study is that centchroman has got 5% failure rates while combined and triphasic pills were 100% effective. As far as safety is concerned centchroman has got lesser side effects except prolongation of cycles. It is completely devoid of the side effects commonly observed with hormonal pills like nausea, vomiting, breakthrough bleeding, weight gain, acne, cholasma, depression, decreased libido, hypertension, scanty menses, ovarian enlargement and breast dyscomfort.

D I S C U S S I O N

DISCUSSION

Basal lipid levels in normal females are as follows (Harrison).

1. Serum total cholesterol (STC) : 130-229 mg/dl.
2. Serum triglycerides (STG) : 40-172 mg/dl.
3. High density lipoprotein (HDL) : 37-83 mg/dl.
4. Low density lipoprotein (LDL) : 71-164 mg/dl.

In the present work the effect of combined contraceptive pills, triphasic pills and centchroman was studied on various lipid levels in serum and their effectiveness and side effects. STC, STG and HDL levels were estimated by chemical kits while LDL, VLDL and LDL/HDL ratio were calculated by standard formulae.

GROUP A

This group consisted 20 females who were taking combined contraceptive pills (Mala-N : 35 mcg of ethenyl estradiol + 1 mg norethindrone acetate) for 12 months.

SERUM TOTAL CHOLESTEROL

In the present study a rising trend in the levels of STC was observed. Mean basal values of STC was 180.33±6.25 mg/dl and after 12 months of continuous use of combined pills STC became 212.16±10.08 mg/dl. Although both the values were within the normal range with a mean rise of 31.33 mg/dl over basal values.

The concentration of serum cholesterol has been directly related to the risk of coronary artery disease

(CAD). No single level of plasma cholesterol appears to separate those at risk from others since the highest levels of cholesterol the greater the risk still of course, those with the highest levels of cholesterol may not develop CAD and those with the lowest level are not completely immune.

In Wynn's study from England the high estrogen group had a mean cholesterol level of approximately 200 mg/dl which was 25 mg/dl over the mean for control and approximately 6% of the patients had a cholesterol level over the 260 mg/dl. However, in 50 ugm level users the mean level was the same as the controls(Wynn et al, 1979).

In a separate study of women using a wide range of birth control pills, oral contraceptive users had significantly higher mean cholesterol levels ranging from 2-16 mg/dl over those of nonusers at different ages, with the greatest difference in the young oral contraceptive users (Wallace et al, 1979).

Obese women may be more likely to have an increase in serum cholesterol while on the pills (Gershberg, et al, 1976).

Arora et al (1988) studied the effect of 30 mcg/1 mg EE/norethindrone pills on serum cholesterol and found no significant change after 3 and 6 months of pills use.

SERUM TRIGLYCERIDES (STG)

The mean basal STG level of group A was 72.66± 2.58 mg/dl which increased upto 104.16±1.72 mg/dl after 12 months of continuous use of combined pills. Although none of the value was beyond the normal range but still there was significant rise in STG. The mean rise over the basal values was 31.5 mg/dl.

Beck (1973) concluded that all estrogen containing birth control pills will increase fasting serum triglyceride levels. This is an estrogen dose dependent increase and is reflected by an increase in VLDL mainly due to an increased hepatic production of triglycerides.

Roy et al (1980) studied on 100 women whom they didivided among 4 different combination pills groups - two with 50 ugm EE_2 and two with 35 ugmEE_2, none of the woman had an elevation in triglycerides out of normal range. However, the three preparations with a norethindrome type progestogen had a significant increase in the mean triglycerides of approximately 30 mg/dl. One group using 35 ugm EE_2 and 150 mg/dl norgestral had no elevation in mean triglyceride. In none of the groups were the results at 3 months of treatment significantly different from those at 6 months.

Prospective studies have been inconclusive in determining if serum triglyceride elevation is a coronary risk factor. This may be due to the fact that it is difficult to separate hypertriglyceridemia from hypertension, obesity, and glucose intolerance, which often

accompany it and which themselves are separate risk factors (Levy and Feinleib, 1980).

In Wynn's comparative study of lipids in different contraceptive pill users, women on high dose estrogen preparation had the highest triglyceride levels. According to them pills appears to increase liver synthesis of triglyceride by at least two fold, which is also accompanied by an increase in urinary excretion of the triglycerides.

HIGH DENSITY LIPOPROTEINS (HDL)

There was significant decrease in serum HDL levels after 12 months use of Mala-N. The mean decrease over the basal value was 18.5 mg/dl from 37.66 ± 1.86 to 19.16 ± 2.13 mg/dl.

Levy and Feinleib (1980) concluded that elevated levels of HDL are associated with a decreased risk of CAD. Exercise, weight loss and alcohol use all are associated with an increase in HDL. Obesity and smoking decrease HDL. However, HDL is also decreased with age. HDL contains 20-25% of totalm plasma cholesterol and by removing cholesterol from tissues, including the walls of arteries. HDL may have a protective action. The prevalence of CAD at HDL level of 30 mg/dl is double that at 60 mg/dl. This is why it might be important to know if the elevated cholesterol levels are due to increased LDL or HDL. Estrogen preparation increase HDL, progestogens decrease HDL and combination birth control pills may have variable

effects, probably dependent on the relative estrogen, progestogen ratio.

Briggs (1980) found almost all combination products to decrease HDL cholesterol somewhat with 30 ugm EE_2 products those pills with 0.5 mg norethindrone had minimal effect on mean HDL cholesterol, while doubling the dose of progestogen to 1 mg norethindrone decrease th mean HDL levels by 7 mg/dl.

There was significant rise in serum LDL and VLDL levels in these females. The mean rise in LDL levels was 44.3 mg/dl after 12 months of use of Mala-N. The mean rise in VLDL was 6.3 mg/dl after 12 months of use of Mala-N over basal values.

LDL/HDL ratio was also increased in this group. The mean rise was 5.66.

In present study observed side effects were breakthrough bleeding, 40% nausea in 30%, vomiting in 10%, weight gain in 10% cases, decreased libido in 10%, acne cholasma, hypertension, breast discomfort, ovarian enlargement, scanty menses and amenorrhoea in 5% cases. The finding of breakthrough bleeding was consistent with the findings of Dickey (1979) who observed that low dose pills are more commonly associated with this side effect as compared to high dose pills.

GROUP B

This group consisted of 20 females who were taking triphasic pills orthonovum 7-7-7 (7 tab -

Norethindrone 0.5 mg + 35 mcg EE, 7 tab. Norethindrone 0.75 mg + 35 mcg EE, 7 tab. Norethindrone 1.0 mg + 35 mcg EE), for 12 months.

SERUM TOTAL CHOLESTEROL (STC)

On the lipid lipoprotein profile there was gradual and significant rise in STC levels over the basal values when the triphasic pills were continuously used for 12 months. The mean rise was 47.63 mg/dl over the basal values from 175.87±9.95 to 207.50±5.92 mg/dl.

This finding is consistent with findings of Wynn et al (1966), Aurell et al (1966), Zorilla et al (1966), Wynn et al (1971) and Arora et al (1989) (unpublished).

Arora et al (1989) observed a significant rise in serum cholesterol concentration with use of sequential pills in females of reproductive age group while there was no significant rise in menopausal and post menopausal females.

The exact mechanism of lipid disturbance is yet to be discover but according to Stadel (1981) the estrogen appears to decrease the LDL cholesterol and to increase HDL cholesterol but some progestine cause reverse. The importance of such changes in genesis of arterial vascular disease such as myocardial infarction or stroke in users of oral contraceptives is not clear but is cause for concern (Knopp, 1988; Meade, 1988 and Mishell, 1988).

Mean serum triglyceride value of group B showed a definite rise of 56 mg/dl over the basal level from 73.16±4.57 to 129.16±6.27 mg/dl. Although none of female showed hypertriglyceridemia.

These findings are similar to findings of Stocks (1979) who obserbed a significant rise in STC levels from 60 mg/dl to 110 mg/dl with the use of sequential pills for 1 years.

Kolkhoff et al (1982) explained that progesterone increases storage of serum triglyceride due to stimulation of lipoprotein lipase which cause hydrolysis of circulating triglycerides and their consequent storage.

Arora et al (1989) studied effects of sequential hormones in different age group females and found a significant rise in STG levels in females of reproductive age group.

There was a significant fall in serum HDL levels in females taking triphasic pills. The basal values of HDL of group Ba was 38.16±4.70 mg/dl which became 21.83± 1.94 mg/dl after 12 months continuous use of triphasic pills. The mean fall over basal values was 16.33 mg/dl.

This finding correlates well with the observations of Aurell and Crammer (1966).

Kennekens et al (1979) found a significant fall in HDL level in hormone users than in nonusers.

Arora et al (1989) found a significant fall in HDL levels in females of reproductive age group using sequential hormones while no effect was observed in menopausal and post menopausal females.

According to Tikkanen and associates (1981, 1982) Progestins can change the relative amount of total HDL, HDL_2 and HDL_3. It is believed that the HDL_2 fraction provides cardiovascular protection(Miller and co-workers, 1982). Therefore, the estrogen and progestin effects on the specific HDL_2 fraction are of special importance because oral contraceptives may alter a woman's cardiovascular risks even though the total HDL cholesterol values are unchanged. Apparently norethindrone containing oral contraceptives do not alter HDL_2 fraction (Hatcher and associates, 1990; Krauss and colleagues, 1983).

More recently however, Patsch and co-workers (1989) reported that two triphasic formulations containing norethindrone and one containing livonorgestral all had similar effects on total HDL, HDL_2 and LDL.

The definitive study is yet to be conducted and may never be. Certainly no final recommendation can be made with respect to livonorgestral containing pills. A prudent choice if lipoproteins are a concern, would be use a low dose norethindrone or possibly a norgestimate containing pill which were recently approved for use.

There was a significant rise in serum LDL and VLDL levels with use of triphasic pills. Triglycerides

and VLDL reflect parallel picture to each other. The mean rise in LDL over basal level was 52.77 mg/dl and in VLDL was 10.77 mg/dl.

The mean rise in LDL/HDL ratio was 4.88 over the basal value.

The findings are consistant with the work done by Aurell et al (1966), Molitch et al (1974), Gupta et al (1976) and Arora et al (1989).

Kauppinen-Makelin and colleagues (1992) noted adverse changes in LDL/HDL ratio as a consequence of 19-nortestosterone progestine and these changes are likely related to the specific progestin and its dose.

As association between oral contraceptives and hypertension became apparent in the late 1960's when several reports appeared of occasional women who while using an estrogen progestin became overtly hypertensive. Oral contraceptive presumably in response to estrogen were shown to increase in plasma angiotensinogen (Renin substrate) to levels near those found in normal pregnancy. Progestin appears to contribute to the hypertension. Weir (1982) observed that women who developed hypertension while taking combined pills and who become normotensive after stopping it and again when progestin only pills employed they redeveloped hypertension.

The risk of hypertension attributable to oral contraceptive pills increases with age (Stadel, 1981).

In present study the observed side effects were nausea in 40% cases, vomiting in 5%, breakthrough bleeding in 25%, weight gain in 15%, depression and decreased libido in 5% cases, breast discomfort and acne in 5% cases.

GROUP C

This group consisted of 40 females using centchroman 30 mg tablet starting one tab on the day of menses and then 2nd tablet on the 4th day then biweekly for the first 3 months on the days they were started (e.g. Sunday, Wednesday if the day of menses was Sunday) and then once weekly dose schedule was followed.

Centchroman is 3,4 trans-2, 2-dimethyl-3 phenyl 4 |p-(beta pyrrolidono-ethoxy) phenyl |. 7-methoxy-chroman hydrochloride a noval nonsteroidal chemical moiety unrelated to any clinically used contraceptive hence possesses no danger of cross reactivity. It exhibits unique combination of weak estrogenic and potent antiestrogenic properties.

Such antiestrogens are expected to exert contraceptives effects by interferring with nidation, an estrogen dependent post ovalatory process. Centchroman appears to manifest its contraceptive action by slightly accelerating embryo transport and suppressing nidation, proliferation for implantation therapy interferring with nidation.

Centchroman does not affect the hypothalamo-pituitary ovarian axis and thus maintains normal ovulatory cycles.

Centchroman estrogenic action is mediated through its interaction with estrogen receptors. However, the mechanism for antagonistic action is not clearly understood. Basic studies with centchroman and its analogoues suggest that a test aminoethoxy moiety when attached to para position on the 4 phenyl substituent increases their relative binding affinity to estradiol receptors.

At the recommended contraceptive doses centchoman does not exhibit progestational, androgenic or antiandrogenic properties, likewise it does not affects the secretion of pituitary, thyroid or adrenal hormones.

In the lipid lipoprotein profile centchroman has got no effect except slight increase in serum HDL level (Mean rise of 3.6 mg/dl over the basal values). While in group A mean rise in STC, STG, LDL, VLDL was 31.83, 31.5, 44.3 and 6.3 mg/dl respectively and ratio of LDL/HDL was raised 5.66 over the basal values after the 12 months of combined pills use.

In the group B there was mean rise in STC, STG, LDL, and VLDL of 47.63, 56.0, 52.77 and 10.47 mg/dl respectively and rise in LDL/HDL ratio was 4.88 and mean fall in HDL was 16.33 mg/dl over the basal values after 12 months use of triphasic pills.

Nityanand et al (1990) observed that centchoman had neither any effect on cholesterol, triglycerides and HDL cholesterol nor it enhanced platelet aggregation. Puri et al (1988) also concluded that centchroman has not effect on lipid lipoprotein profile.

The main observed side effect was prolongation of cycle. The cycle length ranging from 35-50 days. The problem of prolonged cycles was mainly observed during initial 3 months and if the woman tolerate this side effect for first 3 months then afterward the cycles were atmost normal of 30 days duration.

Chandra et al (1981) observed an incidence of 10% of prolonged cycles in their study on 579 women taking centchroman weekly. The pattern of delay was random and not dose related. Most of the cases showed delayed menses resumed, Cycles while on drug treatment. However, some subjects showing a delay of over 90 days, resumed cycles within 40 days of discontinuation of the drug.

Nityanand et al (1990) studied on 125 females and observed that 22.3% cases had one prolonged cycle, 12.9% had 2 prolonged cycles, 13% had more than 2 prolonged cycles.

In present study another observed side effect was scanty menses in 10% cases. The finding is consistent with the study of Chandra et al (1977 and 1981).

Two cases developed pregnancy - one during the initial 2 months of drug therapy and other during initial 6 months of drug therapy.

Nityanand et al (1990) studied on 125 females and observed that out of 19 method failure pregnancies that occurred in 1st clinical studies, 14 occurred in first 6 months of use.

Puri et al (1988) studied 648 females and observed 44 patients failure pregnancies and 19 method failure pregnancies. Out of these 19 method failure, 6 elected for M.T.P., while 13 cases had full term normal deliveries. The follow up of these cases showed normal development of children.

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

In the present study 105 females of reproductive age group were studied. They were divided into study group A (n=20, mean age 26.95±5.11 years, mean weight 51.9±3.44 kg and parity ranging from 0-3) taking combined pills), group B (n=20, mean age 26.25±5.39 years, mean weight 50.95±3.50 kg, parity from 0-3) taking triphasic pills, group C (n=40, mean age 25.92±4.55 years mean weight 52.27±4.0 kg and parity from 0-3) taking centchroman and control group D (n=25, mean age 29.72±6.57 years, mean weight 52.56±3.02 kg, parity from 0-4) not taking any type of hormonal therapy.

The complete general and pelvic examination of each case done at monthly interval for first 3 months then at 6th, 8th and 12th month for evaluation of acceptability, efficacy, safety and changes in lipoprotein profile.

On the lipid lipoprotein profile of group A, there was a significant rise in STC from 180.33±6.25 to 212.61±10.08 mg/dl, a mean rise of 31.5 mg/dl in STG, 44.3 mg/dl in LDL, 6.3 mg/dl in VLDL from basal values observed after 12 months regular use of combined pills.

In group B, there was a significant mean rise in STC (47.63 mg/dl), in STG (56.0 mg/dl), in LDL (52.77 mg/dl) and in VLDL (10.47 mg/dl) over the basal values after 12 months regular use of triphasic pills.

While there was negligible effect of centchroman on lipid profile except a slight mean rise of 3.6 mg/dl in

serum HDL from 36.1±4.7 to 39.7±2.4 mg/dl was observed as compared to significant fall of 18.5 mg/dl in group A and 16.33 mg/dl in group B after 12 months regular use of drug. As far as the acceptability and safety is concern centchroman has got none of the following side effects like nausea, vomiting, breakthrough bleeding, weight gain,, depression, cholasma, acne, decreased libido and hypertension which were commonly experienced with combined and triphasic pills. The only distressing side effect observed with centchroman was prolongation of menstrual cycle ranging from 35 to 50 days in about 25% cases, scanty menses and cervical hypertrophy in about 5% cases. It was observed that none of the patient developed pregnancy during the course of combined or triphasic pills while centchroman has got the method failure rate of 5%.

Thus it is concluded that combined and triphasic pills are 100% effective, while centchroman has got 5% failure rate. But it is totaly devoid of the minor side effects observed with combined and triphasic pills. Although none of the females showed hyperlipidaemia but there was a definite rising trend in lipid levels with combined and triphasic pills. The comparative rise in STC, STG, LDL, VLDL was maximum with triphasic pills, moderate with combined pills and nill with centchroman rather a beneficial effect (rise in HDL) was observed in females taking centchroman as compared to combined and triphasic pills, which causes fall in HDL.

B I B L I O G R A P H Y

BIBLIOGRAPHY

1. Arora et al. Effects of administration and withdrawal of oral contraceptive pills on serummlipids and lipoproteins. Indian J Physiol & Pharmacology, 1988; 32 : 65-71.
2. Aurell M, CramerCC, Rybo G. Serum lipid and lipoprotein during long term administration of an oral contraceptive. Lancet, 1966; 5 : 291-293.
3. Bradley DB, Wingard J, Petitti D et al. Serum high density lipoprotein cholesterol in women using oral contraceptives, estrogen and progesterone. New Engl J Med, 1978; 299 : 17.
4. Beard J, quoted by S.A. Asdell. The growth and function of the corpus luteum. Physiol Rev., 1928;8:313.
5. Briggs MH, Briggs M. Plasma lipoprotein changes during oral contraception. Curr Med Res Opin, 1979; 6 : 249.
6. Briggs NH. Implication and assessments of metabolic effects of oral contraceptives. In New consideration in ora contraceptives. New York, B.M.I. Publications, 1982; 131.
7. Colton FB, Klinstra PD. Oral contraceptives in encyclopedia of chemical technology. John Wiley and Sons Inc New York, 1965; 6 : 62.
8. Beck P : Contraceptive steroids : Modifications of carbohydrate and lipid metabolism. Metabolism 1973, 22 : 841.

9. Dickey RP : Initial pill selection and managing the contraceptive pill patient. Int J Gynaecol Obstet, 1979; 16 : 547.

10. Duncan GW, Lyster SC and Clark JJ. Biologic activities of provest. Endocrinol, 1962; 24:XVII.

11. Farton GMG, Freeman PR, Lawson JP. Oral contraceptives and serum lipids. J Obst Gynaec, 1970; 77 : 551-554.

12. FDA Drug Bull, 1976; 6 : 26, Sequential oral contraceptive removed from market.

13. Gershberg H, Hulse M, Galler M : Serum lipid changes during contraceptive administration in obese women. Relation to serum insulin levels. J Clin Endocrinol Metab 1976; 43 : 861.

14. Goldzieher JW, Moses LE. Study of norethindrone in contraception. JAMA, 1962; 180 : 359.

15. Griffith DR, Williams R, Turner CW. Effect of orally administered progesterone like compound on mammary gland growth in rats. Proc Soc Exptl Biol Med, 1963; 113 : 401.

16. Gupta P, Sharma PK, Sharda S and Nath S : Studies on serum lipids and lipase activity in women using oral contraceptives. Ind J Obst & Gynaec, 1976; 26 :226-9.

17. Hatcher RA, Stewart F, Trussel J, Kowal P, Guest F, Stewart GK, Cates W : Contraceptive technology. 15th edition, New York, Irvington 1990; p 259,262,264,266.

18. Kar AB. Effect of enovid on the response of the ovary of prepubertal rhesus money to exogenous gonadotrophins. Indian J Exp Biol, 1965; 3 : 79.

19. Kahn RH, Baker BL, Zanotti DB : Factors modifying the stimulatory action of norethynodrel on the mammary gland. Endocrinol, 1965; 77 : 162.

20. Kalkhoff RK : Relative sensitivity of post parum gestational diabetic women to oral contraceptive agents and other metabolic stress. Diabetes Care, 1980; 3 : 421.

21. Kamboj VP, Kar AB, Ray S, Grover PK, Anand N. Antifertility activity of centchroman. Indian J Exp Biol 1971; 9 : 103-4.

22. Kauppinen-Makelin R, Kuusi T, Ylikorkala O, Tikkanen MJ : Contraceptives containing desogestrel or levonorgestrel have different effects on serum lipoproteins and postheparin plasma lipase activities. Clin Endocrinol, 1992; 36 : 203.

23. Krauss RM, Roy S, Mishell DR Jr. : Casagranda J, Pike MC : Effects of two low dose oral contraceptives on serum lipids and lipoproteins : Differential changes in high density lipoprotein subclasses. Am J Obstet Gynaecol 1983; 145 : 446.

24. Levy R, Feinleib M; Risk factors for coronary artery disease and their management. In Brownwald E (Ed.) : Heart Disease : A Text book of cardiovascular Medicine - Philadelphia, Saunders, 1980.

25. Maqueo M, Rice Wray E, Calderon JJ, Goldzieber JW: Ocarian morphology after prolonged use of steroid contraceptive agents. Contraception, 1972;5:177.

26. Margueritte White and Jame Mc Greger. Drug therapy Nov., 1991; 58-69.

27. Meade TW : Risks and mechanisms of cardiovascular events in users of oral contraceptives. Am J Obstet 1988; 158 : 1646.

28. Miller NE, Hammett F, Saltissi S, Rao S, Van Zeller H, Coltart J, Lewis B : Relation of angiographically defined coronary artery disease to plasma lipoprotein subfractions and apoproteins. Br Med J 1982; 282:174.

29. Mishell DR Jr, Kletzky OA, Brenner PF, Roy S, Ricoloff J. The effect of contraceptive steroids in hypothalamic pituitary function. Am J Obstet Gynaecol, 1977; 128 : 60.

30. Mishell DR Jr,: Use of oral contraceptives in women of older reproductive age. Am J Obstet Gynaecol, 1988; 158 : 1652.

31. Molitch ME, Oill P and Odell WD : Massive hyperlipidemia during oestrogen therapy. JAMA, 1974; 227 : 522-525.

32. Mukherjee SS, Sethi KI, Srivastava GN, Roy AK, Nityanand S, Mukherjee SK: Chronic toxicity studies of centchroman in rats and rhesus monkeys. Indian J Exp Biol 1977; 15 : 1162-6.

33. Munshi SR, Nair RK, Devi PK : Postcoital contraceptive and uterotrophic effect of centchroman in mice. Indian J Exp Biol 1977; 15 : 1151-3.

34. Pincus G. Effects of progesterone and relative compounds upon reproduction and early development in mammals. Acta Endocrinol Suppl 1956; 28 : 18.

35. Population report No. 8, 1990.

36. Puri V, Kamboj VP, Chandra H, Ray S, Koli PL, Dhawan BN and Anand N : Results of multicentric trial of centchroman. Allied Publishers New Delhi 1988; 436-47.

37. Ramcharan S. The walnut Greek contraceptive drug study : A prospective study of the side effects of oral contraceptives Vol 1, DHEW Publication No. (NIH) Washington, US Govt Printing Office, 1974.

38. Revesz C, Chapel CI, Gandry R : Masculinization of female fetuses in rat by progestational compound. Endocrinology, 1960; 66 : 140.

39. Roy S, Mishell D, Gray G et al: Comparison of metabolic and clinical effects of four oral contraceptives formulations and a contraceptive vaginal ring. Am J Obstet Gynaecol 1980; 136 : 920.

40. Royal Colleges of General practitioners : Oral contraceptives and Health, New York, Pitman, 1974.

41. Scholer HLF, Wachter AM : Evaluation of androgenic properties of progestational compound in rats by foetal (female) masculinization test. Acta Endocrinol, 1961; 38 : 128.

42. Singh MM, Wadhwa V, Kamboj VP : effect of centchroman on ovarian responsiveness to exogenous gonadotrphins in immature female rats. Indian J Exp Biol, 1982; 20 : 448-451.

43. S. Nityanand et al : Clinical evaluation of centchroman A new oral contraceptive proceedings of a symposium organized by the Indian Society for the study of Reproduction and fertility and the WHO's special programme of Research Development and Research Training in human Reproduction, Nov. 4, 1988, Bombay, India.

44. Spellacy WN, Kalra PS, Buhi WR, Birk SA : Pituitary and ovarian responsiveness to a graded gonadotrophin releasing factor stimulation test in women using a low dose estrogen or a regular type of oral contraceptive. Am J Obstet Gynaecol 1980; 137 : 109.

45. Stadel BV : Oral contraceptive and cardiovascular disease. N Engl J Med, 1981; 305 : 612; 672.

46. Starup J, Visfeld TJ : Ovarian morphology and pituitary gonadotrophins in serum during and after long term treatment with oral contraceptives. Acta Obstet Gynaecol Scand 1974; 53 : 161.

47. Stern E, Rorsythe AB, Coffelt CF : Steroid contraceptive use and cervical dysplasia. Increased risk of progression. Science, 1977; 196 : 1460.

48. Taylor HB, Irey NS, Norris HJ : Atypical endocervical hyperplasia in women taking oral contraceptives. JAMA 1967; 202 : 135.

49. Tikkanen MJ, Nikkila EA, Kuusi T, Sipinen S : Plasma high density lipoprotein$_2$ (HDL$_2$) and hepatic lipase: Reciprocal changes produced by estrogen and norgestral. J Clin Endocrinol Metab 1982; 54 : 1113.

50. Tikkanen MJ, Nikkila EA, Kuusi T, Sipinen S : Reduction of plasma high density lipoprotein$_2$ cholesterol and increase of post heparin plasma hepatic lipase activity during progestin treatment. Clin Chem Acta 1981; 115 : 63.

51. Wallace RB, Hoover J, Barret-Connor E et al : Altered plasma lipid and lipoprotein levels associated with oral contraceptive and oestrogen use. Lancet 1979; 2 : 111.

52. Wynn V, Doar JWH and Mills GL : Some effects of oral contraceptives serum lipid and lipoprotein levels. Lancet 1966; 2 : 720-723.

53. Wynn V, Adams PW, Godsland I et al : Comparison of effects of different combined oral contraceptive formulations on carbohydrate and lipid metabolism. Lancet 1979; 1 : 1045.

A P P E N D I X

MASTER CHART

Sl. No.	Name	Age (yrs)	Socio-econo-status	Educational status	Ht. (Inch.)	Wt. (kg.)	Dietary habit	Parity	LCB/LA (months)	M/H	Contraceptives	
											Previous	Present
1.	Rekha	22	Middle	Lit.	62	50	V.	Po+o	-	5/30	-	Centch-roman
2.	Geeta	25	Middle	Lit.	61	48	V.	P1+o	9	4/23	-	"
3.	Shobha	26	Middle	Lit.	62	48	V.	P2+o	6	4/28	-	"
4.	Anita	22	Middle	Lit.	61	48	V.	P1+o	8	5/28	-	"
5.	Anjali	26	Middle	Lit.	60	49	V.	P2+o	12	5/30	-	"
6.	Vineeta	22	Middle	Lit.	60	50	N.V.	P1+o	8	3/28	-	"
7.	Sangeeta	25	Middle	Lit.	60	50	V.	P2+o	8	3/28	-	"
8.	Rajani	24	Lower	Lit.	62	48	N.V.	P1+o	12	3/30	-	"
9.	Rachna	21	Upper	Lit.	59	46	N.V.	Po+o	-	4/28	-	"
10.	Mamta	23	Middle	Lit.	59	48	V.	P2+o	18	4/28	IUCD	"
11.	Usha	20	Middle	Lit.	60	48	V.	Po+o	-	5/30	-	"
12.	Sunita	24	Middle	Lit.	62	52	V.	P1+o	18	5/30	-	"
13.	Babita	25	Middle	Lit.	62	52	V.	P1+o	12	3/28	-	"
14.	Abada	21	Lower	Lit.	60	54	N.V.	P2+o	24	3/28	IUCD	"
15.	Shweta	26	Upper	Lit.	61	56	N.V.	P1+o	12	3/28	-	"
16.	Rashmi	24	Midele	Lit	62	56	N.V.	P1+o	12	3/28	-	"
17.	Rachana	26	Middle	Lit.	62	60	V.	P1+o	18	4/30	IUCD	"
18.	Neeta	27	Middle	Lit.	60	55	V.	P1+o	18	4/30	IUCD	"
19.	Nargish	28	Middle	Lit.	60	54	V.	P1+o	12	4/28	-	"
20.	Meena	30	Middle	Lit.	60	50	V.	Po+o	-	4/30	-	"
21.	Manju	20	Middle	Lit.	61	48	NoV.	Po+o	-	5/30	-	"
22.	Savitri	21	Middle	Lit.	62	54	N.V.	Po+o	-	4/28	-	"
23.	Anjana	22	Middle	Lit.	62	56	V.	Po+o	-	3/30	-	"
24.	Arti	24	Middle	Lit.	63	58	N.V.	P1+o	12	2/30	-	"
1	2	3	4	5	6	7	8	9	10	11	12	13

1	2	3	4	5	6	7	8	9	10	11	12	13
25.	Rajkumari	32	Lower	Lit.	61	64	N.V.	P1+0	12	3/30	-	"
26.	Munni	28	Lower	Lit.	61	55	N.V.	P1+0	24	4/28	-	"
27.	Parwati	36	Middle	Lit.	60	58	N.V.	P1+0	24	4/30	-	"
28.	Kamla	24	Middle	Lit.	59	50	N.V.	P2+0	30	5/30	IUCD	"
29.	Shanti	37	Middle	Lit.	60	60	N.V.	P2+0	18	5/30	"	"
30.	Phoolwati	40	Lower	Illi.	59	62	V.	P3+0	12	4/30	Mala-N	"
31.	Shanti	26	Middle	Lit.	62	54	V.	P2+0	8	4/30	-	"
32.	Reeta	21	Middle	Lit.	63	54	V.	P1+1	4	3/30	-	"
33.	Ranjana	24	Middle	Lit.	62	52	N.V.	P1+0	9	2/30	-	"
34.	Anju	28	Middle	Lit.	60	54	N.V.	P3+0	12	5/30	IUCD	"
35.	Neelam	26	Middle	Lit.	61	53	N.V.	P2+0	6	5/28	-	"
36.	Nisha	30	Middle	Lit.	60	50	V.	P3+0	9	5/28	IUCD	"
37.	Sudha	32	Middle	Lit.	60	46	N.V.	P3+0	12	4/28	"	"
38.	Deepti	26	Middle	Lit.	61	48	N.V.	P1+0	06	3/30	-	"
39.	Gayatri	25	Middle	Lit.	61	52	V.	P1+0	12	3/28	-	"
40.	Ragini	28	Middle	Lit.	62	51	N.V.	P2+0	24	4/30	IUCD	"
41.	Bharti	27	Middle	Lit.	61	52	N.V.	P1+0	8	4/28	-	Mala-N
42.	Gomati	24	Lower	Illit.	64	55	N.V.	P0+0	-	2/30	-	"
43.	Vibha	21	Middle	Lit.	62	55	N.V.	P0+0	-	3/30	-	"
44.	Mini	22	Middle	Lit.	56	54	V.	P0+0	-	3/30	-	"
45.	Deepa	28	Middle	Lit.	59	53	V.	P1+0	8	5/28	-	"
46.	Kamlesh	40	Middle	Lit.	60	61	V.	P2+0	36	4/28	IUCD	"
47.	Archana	21	Middle	Lit.	62	52	V.	P0+0	-	4/30	-	Orthonovum
48.	Nanda	22	Middle	Lit.	62	53	N.V.	P1+0	36	5/30	IUCD	"
49.	Vandana	24	Middle	Lit.	61	54	N.V.	P2+0	24	3/30	-	"
50.	Vijaya	30	Middle	Lit.	62	52	V.	P3+0	72	6/30	IUCD	"
51.	Pushpa	36	Middle	Lit.	62	55	N.V.	P2+0	36	6/28	"	"

1	2	3	4	5	6	7	8	9	10	11	12	13
52.	Asha	28	Middle	Lit.	61	52	V.	P2+o	6	6/30	-	Orthonovum
53.	Santosh	24	Low	Illit.	62	53	N.V.	P2+o	8	5/30	-	Mala-N
54.	Lata	36	Low	Lit.	62	53	V.	P3+o	60	6/28	IUCD	"
55.	Rani	32	Low	Lit	62	46	N.V.	P2+o	36	6/28	"	"
56.	Vidya	28	Low	Illit.	59	48	N.V.	P2+o	8	4/28	-	"
57.	Ganeshi	26	Low	Lit.	59	51	V.	P1+o	12	4/28	-	"
58.	Reema	24	Middle	Lit.	60	52	V.	P1+o	36	6/28	IUCD	"
59.	Nurjahan	26	Low	Illit.	60	50	V.	P1+o	24	5/28	"	"
60.	Sarika	22	Upper	Lit.	61	48	N.V.	P1+o	6	3/30	-	"
61.	Meeta	26	Middle	Lit.	61	54	V.	P2+o	9	4/28	-	Orthonovum
62.	Sukhbinda	30	Middle	Lit.	64	60	N.V.	P3+o	60	5/30	IUCD	"
63.	Shabana	21	Middle	Lit.	60	50	V.	Po+o	-	5/30R	-	"
64.	Kavita	24	Middle	Lit.	61	52	V.	P1+o	6	6/30R	-	"
65.	Leena	26	Middle	Lit.	61	53	V.	P1+o	8	4/30R	-	"
66.	Beni Bai	38	Low	Illit.	62	46	V.	$P2^{+}o$	12	5/30R	IUCD	"
67.	Rahisa	36	Low	Illit.	60	48	V.	$P3\bar{+}o$	48	6/28R	"	"
68.	Manorama	26	Middle	Lit.	60	48	N.V.	P2+o	36	6/28R	"	"
69.	Sarita	21	Middle	Lit.	58	50	N.V.	Po+o	-	5/30R	-	"
70.	Manisha	24	Middle	Lit.	58	46	V.	P1+o	24	6/30R	IUCD	"
71.	Poonam	20	Middle	Lit.	62	48	V.	Po+o	-	5/30R	-	"
72.	Chanda	22	Middle	Lit.	59	50	V.	P1+o	18	4/28R	-	"
73.	Nausheen	28	Middle	Lit.	60	46	V.	P2+o	30	3/30R	-	"
74.	Varsha	22	Middle	Lit.	62	50	V.	P1+o	6	3/28R	-	"
75.	Neeti	23	Upper	Lit.	64	52	N.V.	P1+o	4	5/28R	-	Mala-N
76.	Manjari	24	Middle	Lit.	62	55	V.	P2+o	8	4/28R	-	"
78.	Chandrakala	26	Middle	Lit.	60	46	V.	P2+o	6	3/30R	-	"
78.	Monika	28	Middle	Lit.	62	51	V.	P2+o	30	4/28R	IUCD	"

1	2	3	4	5	6	7	8	9	10	11	12	13
79.	Nikhat	29	Low	Illit.	61	51	N.V.	P3+0	36	6/30R	IUCD	Mala-N
80.	Laxmi	34	Middle	Lit.	61	52	V.	P3+0	36	5/30R	"	"
81.	Madhu	30	Middle	Lit.	61	58	N.V.	P1+0	6	6/30R	-	-
82.	Rashida	36	Low	Lit.	59	52	N.V.	P1+0	8	4/28R	-	-
83.	Lad Kunwar	38	Low	Illit.	59	52	N.V.	P1+0	8	5/30R	-	-
84.	Sushila	20	Low	Lit.	60	51	V.	P1+1	4	3/30R	-	-
85.	Madhuri	22	Middle	Lit.	62	53	V.	P1+2	8	5/30R	-	-
86.	Shashi	28	Middle	Lit.	61	53	V.	P4+0	72	4/28R	IUCD	Ligated
87.	Dayawati	36	Low	Illit.	61	52	V.	P3+0	48	4/30R	Mala-N	"
88.	Krishna	38	Low	Illit.	62	60	N.V.	P2+0	12	3/30R	-	IUCD
89.	Shakun	24	Low	Lit.	59	52	N.V.	P2+0	8	3/32R	-	"
90.	Nanhi	32	Low	Lit.	60	51	V.	P2+0	36	4/32R	Mala-N	Ligated
91.	Nirmala	26	Low	Lit.	61	54	V.	P3+0	72	5/30R	"	"
92.	Kalpana	24	Middle	Lit.	62	53	V.	P3+0	6	4/28R	"	IUCD
93.	Raja Bai	41	Low	Illit.	62	56	N.V.	P1+1	6	3/30R	-	"
94.	Ramwati	40	Low	Illit.	61	58	N.V.	P2+1	48	2/30R	-	Ligated
95.	Uma Devi	30	Middle	Lit.	60	52	N.V.	P3+0	24	3/28	-	"
96.	Basanti	26	Middle	Lit.	59	51	V.	P1+0	9	6/30R	-	-
97.	Bhanumati	38	Low	Illit.	59	53	V.	P3+0	24	4/30R	IUCD	Ligated
98.	Kanta	24	Middle	Lit.	60	54	V.	P4+0	48	4/30R	Pills	"
99.	Mithlesh	20	Middle	Lit.	61	52	V.	P4+0	48	5/28R	Condome	"
100.	Saroj	24	Middle	Lit.	62	52	V.	P2+0	60	5/28R	-	IUCD
101.	Aisha	23	Upper	Lit.	62	50	N.V.	P3+0	6	5/28R	-	Ligated
102.	Rita	26	Middle	Lit.	61	51	V.	P4+0	84	4/30R	-	"
103.	Shayama	32	Low	Lit.	62	46	V.	P4+0	60	4/30R	-	"
104.	Shakuntala	30	Low	Lit.	61	48	V.	P3+0	48	3/30	-	"
105.	Nargis	34	Middle	Lit.	61	50	V.	P3+0	72	3/28	-	"

Sl. No.	B.P. (mm Hg)	Hb (gm%)	Urine		STC at month							STG at month						
			Alb.	Sugar	0	1	2	3	6	8	12	0	1	2	3	6	8	12
	14	15	16	16	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1.	110/70	10.2	Nil	Nil	188	188	186	186	185	186	186	62	62	61	61	61	60	60
2.	116/76	10.5	"	"	185	185	185	185	186	186	186	54	53	53	52	52	52	51
3.	120/70	9.5	"	"	185	185	180	180	180	182	182	52	52	52	51	51	51	51
4.	110/80	9.3	"	"	176	176	177	177	178	176	177	68	68	68	68	68	67	67
5.	100/70	10.0	"	"	190	191	191	189	189	189	190	72	72	72	72	72	73	74
6.	120/70	11.6	"	"	181	182	182	182	183	183	183	74	74	74	74	74	75	75
7.	120/80	12.0	"	"	185	185	182	182	183	184	184	82	83	82	82	82	83	83
8.	116/76	10.0	"	"	182	182	180	180	180	181	181	84	82	82	82	81	81	81
9.	110/72	13.0	"	"	188	188	186	186	186	186	186	90	90	89	89	88	88	88
10.	118/80	12.0	"	"	183	183	183	183	183	183	183	87	86	86	86	86	86	85
11.	128/84	11.8	"	"	189	189	188	188	187	187	189	69	69	69	69	70	70	70
12.	124/80	11.0	%	"	181	181	180	181	181	183	183	71	71	70	70	71	71	71
13.	130/80	10.8	"	"	190	191	191	191	190	191	190	74	74	74	74	73	73	73
14.	104/72	10.2	"	"	182	182	180	180	181	181	182	85	85	85	85	86	87	87
15.	110/72	13.0	"	"	185	185	185	186	186	188	188	82	82	82	82	80	80	80
16.	108/70	11.0	"	"	185	185	186	186	187	187	187	86	85	85	85	86	86	86
17.	130/80	12.0	"	"	187	182	182	182	184	184	184	79	79	79	79	82	82	82
18.	120/76	12.6	"	"	186	186	182	182	183	183	183	61	61	61	62	62	62	64
19.	106/70	11.8	"	"	183	184	184	183	183	184	184	92	92	92	90	90	90	90
20.	110/70	10.9	"	"	180	181	181	180	180	180	180	59	59	60	60	58	58	58
21.	120/80	10.6	"	"	188	188	188	188	187	-	-	60	60	62	59	60	-	-
22.	122/80	11.6	"	"	185	185	186	186	188	-	-	62	62	64	63	62	-	-
23.	126/80	12.0	"	"	185	185	186	186	186	-	-	64	64	64	63	64	-	-
24.	110/70	12.2	"	"	176	176	178	178	178	-	-	82	82	82	78	80	-	-
25.	100/70	10.6	"	"	190	190	192	192	192	-	-	80	80	80	80	80	-	-

	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
26.	116/78	10.8	Nil	Nil	185	185	184	184	185	-	-	81	81	81	81	81	-	-
27.	120/80	10.6	"	"	182	182	182	182	183	-	-	72	74	74	76	76	-	-
28.	122/78	11.8	"	"	188	188	188	189	189	-	-	59	59	59	60	60	-	-
29.	126/80	11.0	"	"	189	186	184	185	185	-	-	74	74	74	74	74	-	-
30.	100/70	10.8	"	"	181	182	182	182	182	-	-	86	88	86	86	86	-	-
31.	118/74	10.4	"	"	197	195	195	195	194	-	-	70	72	72	72	72	-	-
32.	120/80	11.2	"	"	182	183	183	184	184	-	-	74	76	76	76	76	-	-
					0	1	2	3	4	5	6	0	1	2	3	4	5	6
33.	124/78	12.0	"	"	188	-	186	-	186	-	187	74	-	75	-	75	-	76
34.	118/80	11.6	"	"	185	-	185	-	185	-	186	82	-	84	-	84	-	84
35.	106/76	10.8	"	"	185	-	184	-	184	-	185	81	-	81	-	81	-	81
36.	130/84	12.6	"	"	176	-	176	-	176	-	174	64	-	64	-	64	-	64
37.	116/80	10.8	"	"	190	-	192	-	190	-	192	65	-	66	-	66	-	64
38.	110/72	10.6	"	"	185	-	185	-	185	-	185	68	-	70	-	71	-	72
39.	100/70	11.0	"	"	182	-	182	-	182	-	184	71	-	72	-	72	-	72
40.	130/80	11.4	"	"	188	-	188	-	188	-	188	74	-	73	-	73	-	74
41.	110/80	10.8	"	"	191	211	-	-	-	220	-	76	78	-	-	-	86	-
42.	118/84	10.2	"	"	186	201	-	-	-	209	-	73	76	-	-	-	84	-
43.	126/80	9.6	"	"	174	184	-	-	-	196	-	76	79	-	-	-	85	-
44.	130/82	10.8	"	"	180	186	-	-	-	198	-	81	83	-	-	-	90	-
45.	100/70	11.4	"	"	174	179	-	-	-	191	-	82	86	-	-	-	94	-
46.	100/80	12.0	"	"	180	189	-	-	-	200	-	86	88	-	-	-	93	-
47.	106/78	12.6	"	"	190	-	212	-	-	219	-	70	-	74	-	-	86	-
48.	108/80	10.4	"	"	182	-	201	-	-	218	-	72	-	79	-	-	90	-
49.	120/80	11.8	"	"	174	-	180	-	-	206	-	84	-	88	-	-	92	-
50.	128/84	11.6	"	"	182	-	192	-	-	214	-	82	-	90	-	-	102	-
51.	106/70	10.4	"	"	180	-	186	-	-	207	-	64	-	71	-	-	82	-
52.	120/86	10.8	"	"	176	-	186	-	-	208	-	68	-	73	-	-	76	-

					0	1	2	3	6	8	12	0	1	2	3	6	8	12
	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
53.	110/72	11.2	"	"	182	184	193	196	200	-	-	72	76	82	90	94	-	- -
54.	124/80	12.0	"	"	185	192	201	205	207	-	-	74	80	86	92	96	-	-
55.	120/82	11.4	"	"	185	191	202	207	209	-	-	76	81	87	95	98	-	-
56.	106/70	11.0	"	"	178	185	191	201	205	-	-	82	86	91	98	100	-	-
57.	126/80	10.8	"	"	179	184	189	200	203	-	-	83	87	92	100	104	-	-
58.	120/84	10.0	"	"	162	170	179	189	194	-	-	84	88	93	101	106	-	-
59.	120/80	10.6	"	"	164	171	182	193	196	-	-	70	86	91	91	94	-	-
60.	110/76	13.6	"	"	172	179	184	195	198	-	-	68	85	85	94	98	-	-
61.	100/70	10.3	"	"	186	202	214	224	230	236	233	66	72	79	90	102	108	118
62.	130/84	11.2	"	"	190	204	206	212	220	225	231	74	78	84	98	112	120	134
63.	110/70	12.4	"	"	176	187	192	203	218	221	222	70	76	85	99	115	122	136
64.	118/74	10.8	"	"	185	192	199	207	220	223	230	74	79	87	103	112	120	130
65.	124/80	9.8	"	"	176	185	196	204	218	221	229	76	82	91	100	118	124	129
66.	130/86	10.6	"	"	184	198	206	210	230	234	238	79	86	94	102	119	125	128
67.	124/82	10.8	"	"	184	188	200	209	215	-	-	74	76	84	90	95	-	-
68.	130/90	11.4	"	"	190	193	202	209	216	-	-	72	80	85	94	99	-	-
69.	126/84	11.2	"	"	176	179	190	198	208	-	-	76	81	90	93	104	-	-
70.	126/80	11.8	"	"	175	179	186	193	205	-	-	82	70	94	99	109	-	-
71.	120/84	11.2	"	"	169	174	182	188	200	-	-	86	94	99	104	112	-	-
72.	124/80	10.2	"	"	158	164	174	182	201	-	-	84	100	102	111	118	-	-
73.	110/70	10.4	"	"	171	171	183	189	205	-	-	70	81	84	95	106	-	-
74.	116/72	9.8	"	"	182	188	192	201	210	-	-	68	75	83	90	104	-	-
75.	118/74	12.8	"	"	192	212	216	218	222	226	229	77	85	88	89	94	100	105
76.	118/76	9.6	"	"	180	201	204	206	208	211	213	73	80	84	86	90	96	102
77.	116/70	10.8	"	"	176	184	189	192	199	201	207	70	74	79	82	86	94	104
78.	116/72	12.2	"	"	180	194	198	202	210	213	216	73	77	83	86	89	95	104

	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
79.	118/74	12.6	Nil	Nil	174	179	182	190	196	197	199	70	73	79	83	87	94	103
80.	112/70	10.8	"	"	180	189	194	199	202	205	209	73	78	82	84	86	93	107
81.	120/80	11.8	"	"	182	-	-	185	185	182	181	80	-	-	78	78	83	82
82.	116/72	11.6	"	"	178	-	-	175	179	177	176	80	-	-	82	82	80	82
83.	116/74	10.8	"	"	190	-	-	191	191	189	190	88	-	-	89	88	88	89
84.	110/70	11.6	"	"	194	-	-	195	192	194	194	90	-	-	92	90	88	92
85.	110/70	12.2	"	"	172	-	-	172	173	122	172	70	-	-	70	73	70	72
86.	120/80	12.0	"	"	188	-	-	186	188	186	188	78	-	-	78	77	77	78
87.	120/80	10.0	"	"	183	-	-	184	182	182	183	78	-	-	76	74	80	78
88.	116/82	10.2	"	"	184	-	-	182	183	183	183	80	-	-	80	80	81	81
89.	118/80	10.4	"	"	184	-	-	182	182	181	184	90	-	-	92	90	88	90
90.	110/70	10.6	"	"	196	-	-	196	192	192	194	88	-	-	86	86	86	90
91.	110/72	10.2	"	"	187	-	-	186	184	186	186	80	-	-	80	82	82	80
92.	110/74	11.6	"	"	190	-	-	190	190	190	188	84	-	-	84	84	82	82
93.	118/72	10.6	"	"	190	-	-	190	190	190	187	86	-	-	84	86	86	84
94.	118/74	10.2	"	"	176	-	-	176	177	174	176	78	-	-	76	76	76	78
95.	124/82	11.2	"	"	172	-	-	174	174	172	172	80	-	-	82	82	80	80
96.	120/80	11.4	"	"	192	-	-	191	192	192	192	77	-	-	74	72	76	76
97.	120/80	11.0	"	"	196	-	-	192	194	196	196	80	-	-	82	84	78	78
98.	110/70	10.8	"	"	176	-	-	172	174	174	174	80	-	-	82	80	80	80
99.	110/70	10.6	"	"	188	-	-	190	190	188	186	82	-	-	82	82	80	78
100.	120/80	10.0	"	"	186	-	-	188	188	190	190	78	-	-	78	78	78	76
101.	118/72	9.8	"	"	176	-	-	176	176	176	176	82	-	-	84	86	86	82
102.	110/70	9.8	"	"	184	-	-	184	184	184	186	84	-	-	82	82	84	88
103.	110/70	11.0	"	"	182	-	-	182	182	182	182	80	-	-	82	82	84	80
104.	112/72	11.2	"	"	176	-	-	174	174	174	174	79	-	-	80	82	80	80
105.	116/72	10.8	"	"	194	-	-	194	192	194	196	90	-	-	92	88	89	90

SL. No.	HDL at month							VLDL at month						
	0	1	2	3	6	8	12	0	1	2	3	6	8	12
	32	33	34	35	36	37	37	39	40	41	42	43	44	45
1.	36	36	37	37	39	40	42	12.4	12.4	12.2	12.2	12.2	12.0	12.0
2.	38	39	39	40	42	42	42	10.8	10.6	10.6	10.4	10.4	10.4	10.2
3.	34	34	36	36	38	40	40	10.4	10.4	10.4	10.2	10.2	10.2	10.2
4.	35	36	37	37	37	38	39	13.6	13.6	13.6	13.6	13.6	13.4	13.4
5.	39	39	40	40	44	44	44	14.4	14.4	14.4	14.4	14.4	14.6	14.8
6.	37	38	38	39	40	40	41	14.8	14.8	14.8	14.8	14.8	15.0	15.0
7.	31	32	32	32	34	36	36	16.4	16.6	16.4	16.4	16.4	16.6	16.6
8.	40	41	41	42	43	44	44	16.8	16.4	16.4	16.4	16.2	16.2	16.2
9.	34	34	34	35	36	37	37	18.0	18.0	17.8	17.8	17.6	17.6	17.6
10.	35	35	36	36	37	38	38	17.4	17.2	17.2	17.2	17.2	17.2	17.0
11.	36	36	37	37	38	38	39	13.8	13.8	13.8	13.8	14.0	14.0	14.0
12.	38	38	39	39	39	39	40	14.2	14.2	14.0	14.0	14.2	14.2	14.2
13.	32	32	33	33	34	35	36	14.8	14.8	14.8	14.8	14.6	14.6	14.6
14.	36	36	36	37	38	38	39	17.0	17.0	17.0	17.0	17.2	17.4	17.4
15.	33	33	34	35	36	37	38	16.4	16.4	16.4	16.4	16.0	16.0	16.0
16.	39	39	38	38	39	39	39	17.2	17.0	17.0	17.0	17.2	17.2	17.2
17.	40	41	42	42	40	40	42	15.8	15.8	15.8	15.8	16.4	16.4	16.4
18.	41	41	42	42	41	42	42	12.2	12.2	12.2	12.4	12.4	12.4	12.8
19.	36	36	37	37	37	38	39	18.4	18.4	18.4	18.0	18.0	18.0	18.0
20.	32	33	34	34	35	35	37	11.8	11.8	12.0	12.0	11.6	11.6	11.6
21.	34	37	39	42	42	-	-	12.0	12.0	12.4	11.8	12.0	-	-
22.	32	34	38	43	44	-	-	12.4	12.4	12.8	12.6	12.4	-	-
23.	33	35	39	42	42	-	-	12.8	12.8	12.8	12.6	12.8	-	-
24.	31	33	38	43	44	-	-	16.4	16.4	16.4	15.6	16.0	-	-
25.	29	31	34	40	41	-	-	16.0	16.0	16.0	16.0	16.0	-	-

	32	33	34	35	36	37	38	39	40	41	42	43	44	45
26.	31	33	36	40	42	-	-	16.2	16.2	16.2	16.2	16.2	-	
27.	34	36	39	42	42	-	-	14.4	14.8	14.8	15.2	15.2	-	-
28.	32	34	39	42	43	-	-	11.8	11.8	11.8	12.0	12.0	-	-
29.	33	37	39	43	43	-	-	14.8	14.8	14.8	14.8	14.8	-	-
30.	31	34	38	44	44	-	-	17.2	17.6	17.2	17.2	17.2	-	-
31.	32	35	39	44	46	-	-	14.0	14.4	14.4	14.4	14.4	-	-
32.	30	32	36	41	41	-	-	14.8	15.2	15.2	15.2	15.2	-	-
	0	1	2	3	4	5	6	0	1	2	3	4	5	6
33.	39	-	42	-	42	-	42	14.8	-	15.0	-	15.0	-	15.2
34.	38	-	39	-	40	-	40	16.4	-	16.8	-	16.8	-	16.8
35.	42	-	44	-	45	-	45	16.2		16.2	-	16.2	-	16.2
36.	44	-	45	-	48	-	48	12.8	-	12.8	-	12.8	-	12.8
37.	39		42	-	45	-	46	13.0	-	13.2	-	13.2	-	12.8
38.	35	-	37	-	40	-	42	13.6	-	14.0	-	14.2	-	14.4
39.	36	-	38	-	41	-	41	14.2	-	14.4	-	14.4	-	14.4
40.	40	-	42	-	43	-	43	14.8	-	14.6	-	14.6	-	14.8
41.	44	34	-	-	-	27	-	15.2	15.6	-	-	-	17.2	-
42.	40	32	-	-	-	25	-	14.6	15.2	-	-	-	16.8	-
43.	41	40	-	-	-	26	-	15.2	15.8	-	-	-	17.0	-
44.	42	38	-	-	-	23	-	16.2	16.6	-	-	-	18.0	-
45.	35	32	-	-	-	19	-	16.4	17.2	-	-	-	18.8	-
46.	33	30	-	-	-	18	-	17.2	17.6	-	-	-	18.6	-
47.	38	-	31	-	-	19	-	14.0	-	14.8	-	-	17.2	-
48.	41	-	37	-	-	25	-	14.4	-	15.8	-	-	18.0	-
49.	37	-	30	-	-	24	-	16.8	-	17.6	-	-	18.4	-
50.	42	-	38	-	-	34	-	16.4	-	18.0	-	-	20.8	-
51.	35	-	30	-	-	28	-	12.8	-	14.2	-	-	16.4	-
52.	36	-	31	-	-	21	-	13.6	-	14.6	-	-	15.2	-

	0	1	2	3	6	8	12	0	1	2	3	6	8	12
	32	33	34	35	36	37	38	39	40	41	42	43	44	45
53.	32	38	39	42	46	-	-	14.4	15.2	16.4	18.0	18.8	-	-
54.	40	46	45	45	50	-	-	14.8	16.0	17.2	18.4	19.2	-	-
55.	32	40	40	40	49	-	-	15.2	16.2	17.4	19.0	19.6	-	-
56.	32	42	44	46	48	-	-	16.4	17.2	18.2	19.6	20.0	-	-
57.	31	39	42	42	49	-	-	16.6	17.4	18.4	20.0	20.8	-	-
58.	35	42	45	48	52	-	-	16.8	17.6	18.6	20.2	21.2	-	-
59.	32	41	46	49	54	-	-	14.0	17.2	18.2	18.0	18.8	-	-
60.	36	45	46	50	53	-	-	13.6	17.0	17.0	18.8	19.6	-	-
61.	42	40	37	33	31	25	22	13.2	14.4	15.8	18.0	20.4	21.6	23.6
62.	37	35	32	30	28	26	23	14.8	15.6	16.8	19.6	22.4	24.0	26.8
63.	35	30	28	26	24	20	20	14.0	15.2	17.0	19.8	23.0	24.4	27.2
64.	32	30	29	25	23	21	21	14.8	15.8	17.4	20.6	22.4	24.0	26.0
65.	45	40	35	32	29	27	25	15.2	16.4	18.2	20.0	23.6	24.8	25.8
66.	38	36	33	30	25	21	20	15.8	17.2	18.8	20.4	23.8	25.0	25.6
67.	34	30	30	28	24	-	-	14.8	15.2	16.8	18.0	19.0	-	-
68.	32	32	30	26	21	-	-	14.4	16.0	17.0	18.8	19.8	-	-
69.	34	34	30	25	20	-	-	15.2	16.2	18.0	18.6	20.8	-	-
70.	33	30	28	22	19	-	-	16.4	18.0	18.8	19.8	21.8	-	-
71.	29	30	28	24	19	-	-	16.6	18.8	19.8	20.8	22.4	-	-
72.	28	28	26	20	17	-	-	16.8	20.0	20.4	22.2	23.6	-	-
73.	30	31	28	22	16	-	-	14.0	16.2	16.8	19.0	21.2	-	-
74.	31	29	26	20	15	-	-	13.6	15.0	16.6	18.0	20.8	-	-
75.	40	38	32	27	24	24	22	15.4	17.0	17.6	17.8	18.8	20.0	21.0
76.	38	36	30	24	20	20	21	14.6	16.0	16.8	17.2	18.2	19.2	20.4
77.	36	35	30	25	21	20	20	14.0	14.8	15.8	16.4	17.2	18.8	20.8
78.	35	30	27	22	19	17	17	14.6	15.4	16.6	17.2	17.6	19.0	20.8
79.	38	31	29	23	20	17	17	14.0	14.6	15.8	16.6	17.4	18.8	20.6
80.	39	32	30	24	18	18	18	14.6	15.6	16.4	16.8	17.2	18.6	21.4

	32	33	34	35	36	37	38	39	40	41	42	43	44	45
81.	40	-	-	41	40	40	41	16.0	-	-	15.6	15.6	16.6	16.4
82.	47	-	-	46	48	49	49	16.0	-	-	16.4	16.4	16.0	16.4
83.	49	-	-	48	51	51	50	17.6	-	-	17.4	17.6	17.6	17.4
84.	46	-	-	45	47	46	48	18.0	-	-	18.4	18.0	17.6	18.4
85.	40	-	-	49	40	40	41	14.0	-	-	14.0	14.6	14.0	14.4
86.	53	-	-	54	53	54	54	15.6	-	-	15.6	15.4	15.4	15.6
87.	42	-	-	45	44	44	43	15.6	-	-	15.2	14.8	16.0	15.6
88.	46	-	-	45	47	49	47	16.0	-	-	16.0	16.0	16.2	16.2
89.	51	-	-	50	49	51	51	18.0	-	-	17.2	18.0	17.6	18.0
90.	49	-	-	47	51	51	51	17.6	-	-	17.2	17.2	17.2	18.0
91.	43	-	-	42	43	43	43	16.0	-	-	16.0	16.4	16.4	16.0
92.	45	-	-	46	47	47	46	16.8	-	-	16.8	16.8	16.4	16.4
93.	35	-	-	34	35	35	36	17.2	-	-	16.8	17.2	17.2	16.8
94.	40	-	-	42	42	42	42	15.6	-	-	15.2	15.2	15.2	15.6
95.	30	-	-	33	32	30	30	16.0	-	-	16.4	16.4	16.0	16.0
96.	41	-	-	41	45	42	42	15.4	-	-	14.8	14.4	15.2	15.2
97.	47	-	-	45	48	48	47	16.0	-	-	16.6	16.8	15.6	15.6
98.	43	-	-	42	41	45	40	16.0	-	-	14.8	16.0	16.0	16.0
99.	42	-	-	40	43	43	43	16.4	-	-	16.4	16.4	16.0	16.4
100.	30	-	-	32	31	31	30	15.6	-	-	16.4	15.6	15.6	15.2
101.	37	-	-	37	35	37	39	16.4	-	-	16.4	17.2	17.2	16.4
102.	32	-	-	33	32	32	32	16.8	-	-	15.6	16.4	16.8	17.5
103.	39	-	-	37	38	39	40	16.0	-	-	16.8	16.2	16.8	16.0
104.	42	-	-	43	42	45	43	15.8	-	-	16.4	16.4	16.0	16.0
105.	40	-	-	41	39	39	40	18.0	-	-	18.4	17.6	17.8	18.0

Sl. No.	LDL at month							LDL/HDL Ratio at month						
	0	1	2	3	6	8	12	0	1	2	3	6	8	12
	46	47	48	49	50	51	52	53	54	55	56	57	58	59
1.	139.6	139.6	136.8	136.8	133.8	134.0	132.0	3.87	3.87	3.69	3.69	3.43	3.35	3.14
2.	136.2	135.4	135.4	134.6	133.6	133.6	133.8	3.58	3.47	3.47	3.36	3.18	3.18	3.18
3.	140.6	140.6	133.6	133.8	131.8	131.8	131.8	4.13	4.13	3.71	3.71	3.63	3.29	3.29
4.	127.4	126.4	126.4	126.4	127.4	124.4	124.6	3.64	3.51	3.41	3.41	3.44	3.27	3.19
5.	136.6	137.6	136.6	134.6	130.6	130.4	131.2	3.50	3.52	3.41	3.36	2.96	2.96	2.98
6.	129.2	129.2	129.2	128.2	128.2	128.0	125.0	3.49	3.49	3.40	3.28	3.20	3.20	3.20
7.	137.6	136.4	133.6	131.6	132.6	131.4	131.4	4.43	4.26	4.17	4.11	3.90	3.65	3.47
8.	125.2	124.6	122.6	127.6	120.8	120.8	120.8	3.13	3.03	2.99	3.03	2.80	2.74	2.98
9.	136.0	136.0	134.2	130.2	130.4	131.4	128.4	4.00	4.00	3.94	3.72	3.67	3.55	3.47
10.	130.6	130.8	129.8	129.8	128.8	127.8	134.0	3.73	3.73	3.60	3.70	3.48	3.36	3.52
11.	139.2	139.2	137.2	137.2	135.0	135.0	136.0	3.86	3.86	3.70	3.70	3.55	3.55	3.48
12.	128.8	128.8	127.0	128.0	127.8	129.8	128.8	3.38	3.38	3.25	3.87	3.27	3.32	3.22
13.	143.2	144.2	143.2	143.2	141.4	141.4	139.4	4.47	4.50	4.33	3.87	4.15	4.04	3.87
14.	129.0	129.0	127.0	126.0	125.8	126.6	125.6	3.97	3.58	3.52	3.60	3.31	3.30	3.22
15.	135.6	135.6	134.6	134.6	134.0	135.0	134.0	4.10	4.10	3.95	3.54	3.72	3.64	3.52
16.	128.8	129.0	131.0	131.0	130.8	130.8	130.8	3.30	3.30	3.44	3.96	3.35	2.66	3.35
17.	131.2	125.2	124.2	124.2	127.6	127.6	125.6	3.28	3.05	2.95	2.95	3.19	3.19	2.99
18.	132.8	132.8	127.8	127.6	129.6	128.6	128.2	3.23	3.23	3.04	3.03	3.16	3.06	3.05
19.	128.6	129.6	128.6	128.0	128.0	128.0	127.0	3.57	3.60	3.47	3.45	3.45	3.36	3.25
20.	136.2	136.2	135.0	134.0	133.4	133.4	131.4	3.57	4.12	3.97	3.94	3.81	3.81	3.63
21.	142.0	139.0	136.6	134.2	133.0	-	-	4.17	3.75	3.50	3.79	3.16	-	-
22.	140.6	141.6	135.2	130.4	131.6	-	-	4.39	4.16	3.55	3.03	2.99	-	-
23.	139.2	137.2	134.2	131.4	131.2	-	-	4.21	3.92	3.44	3.12	3.15	-	-
24.	128.6	126.6	123.6	119.4	118.0	-	-	4.14	3.83	3.25	2.77	2.68	-	-
25.	145.0	143.0	142.0	136.0	135.0	-	-	5.00	4.61	4.17	3.40	3.29	-	-

	46	47	48	49	50	51	52	53	54	55	56	57	58	59
26.	137.0	135.8	131.8	128.8	126.8	-	-	4.44	4.11	3.66	3.22	3.01	-	-
27.	133.6	131.2	128.2	128.0	125.8	-	-	3.92	3.64	3.28	3.20	2.99	-	-
28.	144.2	142.2	137.2	132.2	134.2	-	-	4.50	4.18	3.51	3.14	3.11	-	-
29.	141.2	134.2	130.2	124.8	127.2	-	-	4.27	3.62	3.33	2.90	2.95	-	-
30.	132.8	130.4	126.8	123.6	120.8	-	-	4.28	3.83	3.33	2.80	2.72	-	-
31.	151.0	145.6	141.6	136.6	133.6	-	-	4.17	4.16	3.63	3.10	2.90	-	-
32.	137.2	135.9	131.8	127.8	127.8	-	-	4.57	4.24	3.66	3.11	3.11	-	-
	0	1	2	3	4	5	6	0	1	2	3	4	5	6
33.	134.2	-	129.0	-	129.0	-	129.8	3.44	-	3.07	-	3.07	-	3.09
34.	130.6	-	129.2	-	128.2	-	129.2	3.43	-	3.31	-	3.20	-	3.23
35.	126.8	-	123.8	-	122.8	-	123.8	3.00	-	2.81	-	2.72	-	2.75
36.	119.2	-	118.2	-	115.2	-	113.2	2.70	-	2.62	-	2.40	-	2.35
37.	138.0	-	136.8	-	131.8	-	133.2	3.53	-	3.25	-	2.92	-	2.89
38.	136.4	-	134.0	-	130.8	-	128.6	3.89	-	3.62	-	3.27	-	3.06
39.	131.8	-	129.6	-	126.6	-	128.6	3.66	-	3.41	-	3.08	-	3.13
40.	133.2	-	131.4	-	130.4	-	130.2	3.33	-	3.12	-	3.03	-	3.02
41.	131.8	161.4	-	-	-	175.8	-	2.79	4.74	-	-	-	6.48	-
42.	131.4	153.8	-	-	-	167.2	-	3.28	4.80	-	-	-	6.68	-
43.	117.8	128.2	-	-	-	153.0	-	2.87	3.20	-	-	-	5.88	-
44.	121.8	131.4	-	-	-	157.0	-	2.90	3.45	-	-	-	6.82	-
45.	122.6	129.4	-	-	-	153.2	-	3.50	4.05	-	-	-	8.06	-
46.	129.8	141.4	-	-	-	163.4	-	3.90	4.71	-	-	-	9.07	-
47.	138.0	-	166.2	-	-	182.8	-	3.63	-	5.36	-	-	9.62	-
48.	126.6	-	148.2	-	-	175.0	-	3.08	-	4.00	-	-	7.00	-
49.	120.2	-	132.4	-	-	163.6	-	3.24	-	4.41	-	-	6.81	-
50.	123.6	-	136.0	-	-	159.2	-	2.94	-	3.57	-	-	4.68	-
51.	132.2	-	141.8	-	-	162.6	-	3.77	-	4.72	-	-	5.80	-
52.	126.4	-	140.4	-	-	171.8	-	3.51	-	4.52	-	-	8.18	-

	0	1	2	3	6	8	12	0	1	2	3	6	8	12
	46	47	48	49	50	51	52	53	54	55	56	57	58	59
53.	135.6	130.8	137.6	136.0	135.2	-	-	4.23	3.44	3.52	3.23	2.93	-	-
54.	130.20	130.0	138.8	141.6	137.8	-	-	3.25	2.88	3.08	3.14	2.75	-	-
55.	137.8	134.8	144.6	148.0	140.4	-	-	4.30	3.37	3.61	3.70	2.86	-	-
56.	129.6	125.8	128.8	135.4	137.0	-	-	4.05	2.99	2.92	2.94	2.85	-	-
57.	131.4	127.6	128.6	138.0	133.2	-	-	4.23	3.27	3.06	3.28	2.71	-	-
58.	110.2	110.4	115.4	128.8	120.8	-	-	3.14	2.62	2.56	2.51	2.32	-	-
59.	118.0	112.8	117.8	126.0	123.2	-	-	3.68	2.50	2.56	2.57	2.28	-	-
60.	122.4	117.0	121.0	126.2	125.4	-	-	3.40	2.60	2.66	2.52	2.36	-	-
61.	130.8	147.6	161.2	173.0	178.6	189.4	187.4	3.11	3.69	4.35	5.24	5.76	7.56	8.51
62.	138.2	153.4	157.2	162.4	169.6	175.0	181.2	3.73	4.38	4.91	5.41	6.05	6.73	7.87
63.	127.0	141.8	147.0	162.2	171.0	176.0	174.8	3.62	4.72	5.25	6.23	7.12	8.80	8.74
64.	138.2	146.2	152.6	161.4	164.6	178.0	183.0	4.31	4.87	5.26	6.45	7.59	8.47	8.71
65.	115.8	128.6	142.8	152.0	165.4	169.2	178.2	2.75	3.21	4.08	4.75	5.72	6.26	7.12
66.	130.2	144.8	154.2	159.6	181.2	188.0	192.4	3.42	4.02	4.67	5.32	7.24	8.95	9.62
67.	135.2	142.8	153.2	163.0	172.0	-	-	3.97	4.76	5.10	5.82	7.16	-	-
68.	143.6	145.0	155.0	164.2	175.2	-	-	4.48	4.53	5.16	6.31	8.34	-	-
69.	126.8	128.8	142.0	154.4	167.2	-	-	3.72	3.78	4.73	6.17	8.36	-	-
70.	125.6	131.0	139.2	151.2	164.2	-	-	3.80	4.36	4.97	6.87	8.64	-	-
71.	123.4	125.2	134.2	143.2	158.6	-	-	4.25	4.17	4.79	5.96	8.34	-	-
72.	113.4	116.0	127.6	139.8	160.4	-	-	4.05	4.14	4.90	6.97	9.43	-	-
73.	127.0	129.8	138.2	148.0	167.8	-	-	4.23	4.18	4.93	6.72	10.48	-	-
74.	137.4	144.0	149.2	163.0	174.2	-	-	4.43	4.96	5.74	8.15	11.60	-	-
75.	136.6	157.0	166.4	173.2	179.2	182.00	186.0	3.41	4.13	5.20	6.41	7.46	7.58	8.45
76.	127.4	149.0	157.2	164.2	170.0	171.8	171.6	3.35	4.13	5.24	6.84	8.50	8.59	8.17
77.	126.0	134.2	143.2	150.6	160.8	162.2	166.2	3.50	3.83	4.77	6.02	7.65	8.11	8.31
78.	128.4	148.6	154.4	162.8	173.2	177.0	178.2	3.66	4.95	5.71	7.40	9.11	10.41	10.48

	46	47	48	49	50	51	52	53	54	55	56	57	58	59
79.	122.0	133.6	137.2	150.4	158.6	161.2	161.4	3.21	4.30	4.73	6.53	7.93	9.48	9.49
80.	126.4	141.6	147.6	158.2	166.8	168.4	169.6	3.24	4.42	4.92	6.59	9.26	9.35	9.42
81.	126.0	-	-	128.4	129.6	125.4	123.6	3.15	-	-	3.13	3.24	3.13	3.01
82.	115.0	-	-	112.6	114.6	107.0	110.6	2.44	-	-	2.44	2.38	2.18	2.25
83.	123.4	-	-	125.6	122.4	120.4	122.6	2.51	-	-	2.61	2.40	2.36	2.45
84.	130.0	-	-	131.6	127.0	130.4	127.6	2.82	-	-	2.92	2.70	2.83	2.65
85.	118.0	-	-	109.0	118.4	118.0	116.6	2.95	-	-	2.22	2.96	2.95	2.84
86.	119.4	-	-	116.4	119.6	116.6	118.4	2.25	-	-	2.15	2.25	2.15	2.19
87.	125.4	-	-	123.8	123.2	122.0	124.4	2.98	-	-	2.75	2.80	2.77	2.89
88.	120.4	-	-	121.0	120.0	117.8	119.8	2.61	-	-	2.42	2.55	2.40	2.54
89.	117.0	-	-	114.8	115.0	112.4	115.0	2.29	-	-	2.29	2.34	2.20	2.25
90.	130.2	-	-	131.8	123.8	103.8	125.0	2.65	-	-	2.80	2.42	2.03	2.45
91.	126.8	-	-	128.0	124.6	126.6	127.0	2.94	-	-	3.04	2.89	2.94	2.95
92.	129.4	-	-	127.2	126.2	126.6	125.6	2.87	-	-	2.76	2.68	2.69	2.73
93.	139.0	-	-	139.2	137.8	137.8	134.4	3.97	-	-	4.09	3.93	3.93	3.72
94.	124.4	-	-	118.8	119.8	116.8	118.4	3.11	-	-	2.82	2.85	2.78	2.81
95.	126.0	-	-	124.6	125.6	126.0	126.0	4.2	-	-	3.77	3.92	4.20	4.20
96.	133.6	-	-	135.2	131.6	134.8	134.8	3.25	-	-	3.29	2.92	3.20	3.20
97.	137.0	-	-	130.6	129.2	132.4	133.4	2.91	-	-	2.90	2.69	2.77	2.83
98.	117.0	-	-	115.2	117.0	113.0	132.0	2.72	-	-	2.74	2.85	2.93	3.30
99.	129.6	-	-	133.6	130.6	129.0	114.6	3.08	-	-	3.34	3.03	2.66	2.66
100.	140.4	-	-	139.6	141.4	143.4	140.8	4.68	-	-	4.36	4.56	4.62	4.69
101.	122.6	-	-	122.6	123.8	121.8	134.6	3.31	-	-	3.31	3.53	3.29	3.45
102.	135.2	-	-	135.4	135.6	135.2	126.5	4.22	-	-	4.10	4.23	4.22	3.95
103.	127.0	-	-	128.2	127.8	126.2	126.0	3.25	-	-	3.46	3.36	3.23	3.15
104.	118.2	-	-	114.6	115.6	113.0	115.0	2.81	-	-	2.66	2.75	2.41	2.67
105.	136.0	-	-	134.6	135.4	137.2	138.0	3.40	-	-	3.28	3.46	3.51	3.45

WORKING PROFORMA

CLINICAL TRIAL OF CENTCHROMAN Vs NORMONAL CONTRACEPTIVE PILLS

Case No._____

Name Age

Address Socio-economic status:

Occupation Educational status : Wife Husband

Combined family Income:

Previous Medical History :

a. During last 1 year

b. Preceding 1 year period

Drug Treatments Drugs Duration

a. During last 1 year

b. Preceding 1 year period

Previous Gynaecological History

a. During last 1 year

b. Preceding 1 year period

Clinical Examination

General

Systemic

Pelvic

Breast

Menstrual History	During last 1 year	Preceding 1 year
Average cycle length		
Duration		
Flow (normal/heavy/scanty)		
Pain (yes/no)		
Regularity		
Any other associated complaint		

Age of Menarche Last Menstrual Periods

Obstetrical History :

Last child birth/Last abortion Elapsed Time

Parity

Nature of Deliveries (Home/Hospital) (Normal/Operative)

Age at first delivery
Duration gap in between deliveries
Method of contraception
Pills
Name
Duration
Break in Use Period Reason
Any side effect

Present Contraceptive CENTCHROMAN/MALA/ORTHONOVIN-7-7-7
Date of start Regularity
Regulatity verified by How
Method of use Dose
Method of restart after break
Date, period and reason of break
Duration used

Any side effect or problem

FEATURE	Month	1	2	3	6	8	12 month
PILL USE (REG/IREG)							
MENSES							
Date							
Duration							
Flow							
Pain							
P/V EXAMINATION							
ULTRA-SONOGRAPHY							
Uterus							
Adenexa							
Ovaries							
Follicles(no/maturation)							
Other findings							
Weight (kg)							
B.P.(mm Hg)							
Endometrial Biopsy							

VAGINAL CYTOLOGY

PLASMA LIPOPROTEINS

STC	mg%
HDL-c	mg%
LDL-c	mg%
VLDL-c	mg%
LDL/HDL ratio	

SIDE EFFECTS

REMARKS

SIGNATURE